

10/524815

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16

FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

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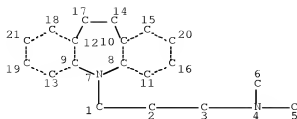
This file contains CAS Registry Numbers for easy and accurate
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'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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L4 STR

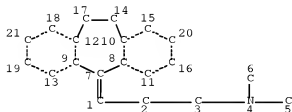
10/524815



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
 L5 STR



NODE ATTRIBUTES:
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10/524815

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OR L15 OR L16)
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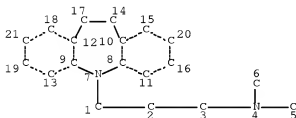
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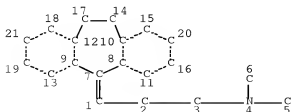
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L87 22 L76 OR L77 OR L84

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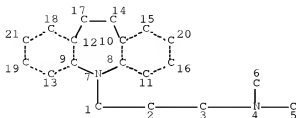
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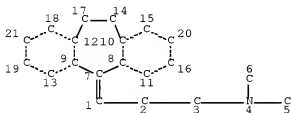
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L47      78135 SEA L46
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L53      91067 SEA L52
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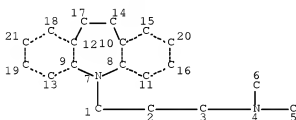
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L79      48 SEA L75 AND L29

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L4 STR



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STEREO ATTRIBUTES: NONE
 L5 STR

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L56 24 SEA (TRICYCLIC OR TETRACYCLIC)/BI AND L29
L57 75 SEA L49 OR L54 OR L56
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L82 8 SEA L57 AND L75

=> s L78 or L79 or L82
L88 64 L78 OR L79 OR L82

=> dup rem L87 L88
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PROCESSING COMPLETED FOR L87
PROCESSING COMPLETED FOR L88
L89 37 DUP REM L87 L88 (49 DUPLICATES REMOVED)
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ANSWERS '23-29' FROM FILE MEDLINE
ANSWERS '30-32' FROM FILE EMBASE
ANSWERS '33-37' FROM FILE BIOSIS

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L89 ANSWER 1 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2009:173669 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:188953

TITLE: Cystic fibrosis and innate immunity: how chloride channel mutations provoke lung disease

AUTHOR(S): Doering, Gerd; Gulbins, Erich

CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene, Tuebingen, 72074, Germany

SOURCE: Cellular Microbiology (2009), 11(2), 208-216
CODEN: CEMIF5; ISSN: 1462-5814

PUBLISHER: Wiley-Blackwell

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Innate immunity is essential for prevention of infection in vertebrates and plants and dysfunction of single components of innate immunity may provoke severe disease. Here we describe how mutations in the cystic fibrosis transmembrane conductance regulator gene dysregulate a variety of components of the innate immune system in individuals suffering from the hereditary disease cystic fibrosis. In the airways of these individuals, functions of the mucociliary clearance system, cationic antimicrobial (poly)peptides and neutrophils and macrophages are impaired and inflammatory signal transduction pathways exaggerated. Consequently, chronic airway colonization with opportunistic bacterial pathogens develops and leads to life-threatening lung disease.

CC 15-0 (Immunochemistry)

Section cross-reference(s): 14

ST review cystic fibrosis innate immunity chloride channel mutation

IT CFTR (cystic fibrosis transmembrane

conductance regulator)
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (chloride channel mutations provoke lung disease)
 IT Cystic fibrosis
 (cystic fibrosis and innate immunity)
 IT Immunity
 (innate; cystic fibrosis and innate immunity)
 REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 2 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 2
 ACCESSION NUMBER: 2009:829732 ZCAPLUS Full-text
 TITLE: Therapeutic Efficacy and Safety of Amitriptyline in
 Patients with Cystic Fibrosis
 AUTHOR(S): Riethmueller, Joachim; Anthonysamy, Janina; Serra,
 Emilio; Schwab, Matthias; Doering, Gerd; Gulbins,
 Erich
 CORPORATE SOURCE: Department of Paediatrics, University Hospital
 Tuebingen, Tuebingen, D-72076, Germany
 SOURCE: Cellular Physiology and Biochemistry (2009), 24(1-2),
 65-72
 CODEN: CEPBEW; ISSN: 1015-8987
 PUBLISHER: S. Karger AG
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase,
 significantly reduces Pseudomonas aeruginosa lung infection in cystic fibrosis
 (CF) mice with concurrent increase of survival. Our aim was to establish
 whether amitriptyline is safe and effective in the treatment of CF patients.
 In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4
 adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for
 14 days. Subsequently in a phase II study 19 adult CF patients were randomly
 allocated to three treatment groups receiving amitriptyline once daily for 28
 days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13).
 The primary outcome was the difference of forced expiratory volume in 1 s
 (FEV1) at day 14 between amitriptyline and placebo. Primary endpoint measures
 improved significantly in three of four patients in the pilot study after
 amitriptyline treatment vs placebo (relative FEV1: 14.7±5%; p = 0.006) and in
 the 25 mg treatment group of the phase II study (relative FEV1: 4.0±7%; p =
 0.048). Amitriptyline was well tolerated in both studies and 96% of the
 patients completed the studies. Amitriptyline as a novel therapeutic option
 in patients with CF is safe and seems to be efficacious.

CC 1 (Pharmacology)
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 3 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
 ACCESSION NUMBER: 2008:1343334 ZCAPLUS Full-text
 DOCUMENT NUMBER: 150:18250
 TITLE: Ceramide in bacterial infections and cystic fibrosis
 AUTHOR(S): Grassme, Helke; Becker, Katrin Anne; Zhang, Yang;
 Gulbins, Erich
 CORPORATE SOURCE: Department of Molecular Biology, University of
 Duisburg-Essen, Essen, D-45122, Germany
 SOURCE: Biological Chemistry (2008), 389(11), 1371-1379
 CODEN: BICHF3; ISSN: 1431-6730
 PUBLISHER: Walter de Gruyter GmbH & Co. KG
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review. Ceramide is formed by the activity of sphingomyelinases, by degradation of complex sphingolipids, reverse ceramidase activity or de novo synthesized. The formation of ceramide within biol. membranes results in the formation of large ceramide-enriched membrane domains. These domains serve the spatial and temporal organization of receptors and signaling mol's. The acid sphingomyelinase-ceramide system plays an important role in the infection of mammalian host cells with bacterial pathogens such as *Neisseria gonorrhoeae*, *Escherichia coli*, *Staphylococcus aureus*, *Listeria monocytogenes*, *Salmonella typhimurium* and *Pseudomonas aeruginosa*. Ceramide and ceramide-enriched membrane platforms are also involved in the induction of apoptosis in infected cells, such as in epithelial and endothelial cells after infection with *Pseudomonas aeruginosa* and *Staphylococcus aureus*, resp. Finally, ceramide-enriched membrane platforms are critical regulators of the release of pro-inflammatory cytokines upon infection. The diverse functions of ceramide in bacterial infections suggest that ceramide and ceramide-enriched membrane domains are key players in host responses to many pathogens and thus are potential novel targets to treat infections.

CC 14-0 (Mammalian Pathological Biochemistry)

ST review ceramide infection bacteria cystic fibrosis

IT Bacterial infection
Cell membrane
Cystic fibrosis
Escherichia coli
Human
Listeria monocytogenes
Mycobacterium
Neisseria gonorrhoeae
Pseudomonas aeruginosa
Salmonella typhimurium
Staphylococcus aureus
(ceramide in bacterial infections and cystic fibrosis)

IT Ceramides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide in bacterial infections and cystic fibrosis)

IT 9031-54-3, Sphingomyelinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide in bacterial infections and cystic fibrosis)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 4 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2009:58346 ZCAPLUS Full-text

DOCUMENT NUMBER: 150:559646

TITLE: Sphingolipids in the lungs

AUTHOR(S): Uhlig, Stefan; Gulbins, Erich

CORPORATE SOURCE: Institute of Pharmacology and Toxicology, University
Hospital Aachen, RWTH Aachen, Aachen, Germany

SOURCE: American Journal of Respiratory and Critical Care
Medicine (2008), 178(11), 1100-1114
CODEN: AJCMED; ISSN: 1073-449X

PUBLISHER: American Thoracic Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Sphingolipids such as sphingosine-1-phosphate (S1P), ceramide, or sphingomyelin are essential constituents of plasma membranes and regulate many

(patho)physiol. cellular responses inducing apoptosis and cell survival, vascular permeability, mast cell activation, and airway smooth muscle functions. The complexity of sphingolipid biol. is generated by a great variety of compds., diverse receptors, and often antagonistic functions of different sphingolipids. For instance, apoptosis is promoted by ceramide and prevented by S1P, and pulmonary vascular permeability is increased by S1P2/3 receptors and by ceramide, whereas S1P1 receptors stabilize barrier integrity. Several enzymes of the sphingolipid metabolism respond to external stimuli such as sphingomyelinase isoenzymes that are activated by many stress stimuli and the sphingosine kinase isoenzymes that are activated by allergens. The past years have provided increasing evidence that these processes contribute to pulmonary disorders including asthma, chronic obstructive pulmonary disease, acute lung injury, and cystic fibrosis. Sphingolipid metabolism offers several novel therapeutic targets for the treatment of lung diseases such as emphysema, asthma, cystic fibrosis, respiratory tract infection, sepsis, and acute lung injury.

CC 14-0 (Mammalian Pathological Biochemistry)

IT Respiratory system disease

(infection; sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Infection

(respiratory tract; sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Stress, biological

(sphingolipid metabolic sphingomyelinase isoenzyme activated by stress stimulus contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

IT Allergens

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid metabolic sphingosine kinase isoenzyme activated by allergen contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

IT Asthma

Cystic fibrosis

Emphysema

Human

Smooth muscle

(sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Sphingolipids

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid receptors have role in airway smooth muscle function and its metabolism contributes for chronic lung disorders like asthma, emphysema, cystic fibrosis and respiratory tract infection in human)

IT Ceramides

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(sphingolipid such as ceramide contributes for lung disorders like emphysema, cystic fibrosis, cystic

- fibrosis and respiratory tract infection in human)
- IT Sphingomyelins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingolipid such as sphingomyelin contributes for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)
- IT Apoptosis
(sphingolipid such as sphingomyelin, sphingosine-1-phosphate and ceramide regulates cellular responses inducing apoptosis and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT Mast cell
(sphingolipid such as sphingomyelin, sphingosine-1-phosphate and ceramide regulates cellular responses inducing mast cell activation and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT Vascular permeability
(sphingolipid such as sphingomyelin, sphingosine-1-phosphate and ceramide regulates cellular responses inducing vascular permeability and contributes for emphysema, cystic fibrosis and respiratory tract infection in human)
- IT 9031-54-3, Sphingomyelinase
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingolipid metabolic sphingomyelinase isoenzyme activated by stress stimulus contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)
- IT 50864-48-7, Sphingosine kinase
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingolipid metabolic sphingosine kinase isoenzyme activated by allergen contributing for lung disorders like emphysema, cystic fibrosis, cystic fibrosis and respiratory tract infection in human)

REFERENCE COUNT: 189 THERE ARE 189 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 5 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2008:1496580 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 150:205817

TITLE: Influence of amitriptyline on erythrocyte, parasitemia and survival of Plasmodium berghei-infected mice

AUTHOR(S): Brand, Verena; Koka, Saisudha; Lang, Camelia; Jendrossek, Verena; Huber, Stephan M.; Gulbins, Erich; Lang, Florian

CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Germany

SOURCE: Cellular Physiology and Biochemistry (2008), 22(5-6), 405-412

CODEN: CEPBEW; ISSN: 1015-8987

PUBLISHER: S. Karger AG

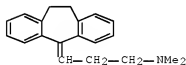
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Plasmodia express a sphingomyelinase, which is apparently required for their development. On the other hand, the sphingomyelinase product ceramide has previously been shown to delay parasite development. Moreover, ceramide triggers suicidal erythrocyte death or erythrocyte, characterized by exposure of

phosphatidylserine at the erythrocyte surface and cell shrinkage. Accelerated eryptosis of infected erythrocytes is considered to clear infected erythrocytes from circulating blood and, thus, to favorably influence the clin. course of malaria. The present expts. explored whether the sphingomyelinase inhibitor amitriptyline or genetic knockout of host acid sphingomyelinase influence in vitro parasite growth, eryptosis of *Plasmodium falciparum*-infected human erythrocytes, in vivo parasitemia and survival of *P. berghei*-infected mice. Phosphatidylserine exposure was determined by annexin V-binding and cell volume by forward scatter in FACS anal. In vitro infection of human erythrocytes increased annexin-binding, an effect blunted in the presence of amitriptyline ($\geq 50 \mu\text{M}$). Amitriptyline did not significantly alter intraerythrocytic parasite development but significantly ($\geq 1 \mu\text{M}$) delayed the increase in parasitemia in vitro. Most importantly, amitriptyline treatment (1 mM in drinking water) resulted in a significant delay of parasitemia and death of infected mice. However, upon infection, ceramide formation was stimulated in both, acid sphingomyelinase knockout mice (*Smpd1*^{-/-}) and their wild type littermates (*Smpd1*^{+/+}). Parasitemia following *P. berghei* infection was significantly lower in *Smpd1*^{-/-} than in *Smpd1*^{+/+} mice but did not significantly extend the life span of infected animals. In conclusion, mammalian and parasite sphingomyelinase contribute to ceramide formation during malaria, whereby the parasite sphingomyelinase ultimately detcs. the course of the infection. Amitriptyline presumably blocks both sphingomyelinases and, thus, its use might be a novel strategy to treat malaria.

CC 1-5 (Pharmacology)
 IT 50-48-6, Amitriptyline
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amitriptyline inhibits host and parasite sphingomyelinase in *Plasmodium berghei*-infected mice)
 IT 50-48-6, Amitriptyline
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amitriptyline inhibits host and parasite sphingomyelinase in *Plasmodium berghei*-infected mice)
 RN 50-48-6 ZCAPLUS
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)
 REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 6 OF 37 ZCAPLUS COPYRIGHT 2009 ACS ON STN DUPLICATE 7
 ACCESSION NUMBER: 2008:439128 ZCAPLUS Full-text
 DOCUMENT NUMBER: 149:6518
 TITLE: Ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis

AUTHOR(S): Teichgraeber, Volker; Ulrich, Martina; Endlich, Nicole; Riethmueller, Joachim; Wilker, Barbara; De Oliveira-Munding, Cheyla Conceicao; van Heeckeren, Anna M.; Barr, Mark L.; von Kuerthy, Gabriele; Schmid, Kurt W.; Weller, Michael; Tuemmler, Burkhard; Lang, Florian; Grassme, Heike; Doering, Gerd; Galbins, Erich

CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Essen, 45122, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2008), 14(4), 382-391
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microbial lung infections are the major cause of morbidity and mortality in the hereditary metabolic disorder cystic fibrosis, yet the mol. mechanisms leading from the mutation of cystic fibrosis transmembrane conductance regulator (CFTR) to lung infection are still unclear. Here, we show that ceramide age-dependently accumulates in the respiratory tract of uninfected CFtr-deficient mice owing to an alkalization of intracellular vesicles in CFtr-deficient cells. This change in pH results in an imbalance between acid sphingomyelinase (Asm) cleavage of sphingomyelin to ceramide and acid ceramidase consumption of ceramide, resulting in the higher levels of ceramide. The accumulation of ceramide causes CFtr-deficient mice to suffer from constitutive age-dependent pulmonary inflammation, death of respiratory epithelial cells, deposits of DNA in bronchi and high susceptibility to severe Pseudomonas aeruginosa infections. Partial genetic deficiency of Asm in CFtr-/Smpdl+/- mice or pharmacol. treatment of CFtr-deficient mice with the Asm blocker amitriptyline normalizes pulmonary ceramide and prevents all pathol. findings, including susceptibility to infection. These data suggest inhibition of Asm as a new treatment strategy for cystic fibrosis.

CC 14-4 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

ST ceramide inflammation infection susceptibility cystic fibrosis

IT Cystic fibrosis

Human

Pneumonitis

Pseudomonas aeruginosa

Respiratory system

(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

IT CFTR (cystic fibrosis transmembrane conductance regulator)

Ceramides

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

IT Sphingomyelins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

IT DNA

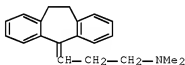
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(deposits in respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)

IT Respiratory system

(epithelium, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic

- fibrosis)
- IT Apoptosis
(of respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Epithelium
(respiratory tract, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Organelle
(vesicle, alkalization of; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 57-88-5, Cholesterol, biological studies 123-78-4, Sphingosine 9031-54-3, Acid sphingomyelinase 26993-30-6, Sphingosine 1-phosphate 37289-06-8, Acid ceramidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 212059-03-5, Peptamen
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 7 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 8
 ACCESSION NUMBER: 2008:1066216 ZCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 149:439268
 TITLE: DNA Quantification and Fragmentation in Sputum after Inhalation of Recombinant Human Deoxyribonuclease
 AUTHOR(S): Riethmueller, Joachim; Vonthein, Reinhard; Borth-Bruhns, Thomas; Grassme, Heike; Eyrich, Matthias; Schilbach, Karin; Stern, Martin; Gulbins, Erich

10/524815

CORPORATE SOURCE: Department of Pediatrics, Tuebingen University
Hospital, Tuebingen, D-72076, Germany

SOURCE: Cellular Physiology and Biochemistry (2008), 22(1-4),
347-352
CODEN: CEPBEW; ISSN: 1015-8987

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inhaled rhdNase may improve sputum viscosity and mucociliary clearance by
cleavage of extracellular DNA derived for instance from dead leukocytes in
purulent, highly viscous patient sputum. Here we established a method to
quantify rhdNase-mediated DNA fragmentation in sputum using gel
electrophoresis. Sputum of *Pseudomonas aeruginosa* colonized cystic fibrosis
(CF) patients with (CF+) or without (CF-) rhdNase treatment or mech.
ventilated non-CF patients receiving rhdNase (non-CF+) or not (non-CF-) was
analyzed. DNA measurements from T-lymphocytes served as controls. Absolute
DNA content and the relative quantity within eight mol. mass ranges (12000 to
200 bp) was determined by gel electrophoresis and densitometric anal.
Geometric mean sputum DNA concns. were 0.41 mg/dL for CF- (n=54), 0.78 mg/dL
for CF+ (n=60), 0.053 mg/dL for non-CF- (n=41) and 0.049 mg/dL for non-CF+
(n=28). Treatment with rhdNase resulted in fragmentation of DNA that was
quantified by separation and densitometric anal. of the DNA on agarose gels.
The new anal. method permits anal. of DNA cleavage with high accuracy. This
new monitoring method facilitates DNA quantification and in vitro monitoring
of rhdNase in sputum.

CC 1-1 (Pharmacology)

IT Cystic fibrosis
DNA fragmentation
Expectorants
Gel electrophoresis
Human
Sputum
Therapeutic drug monitoring
(DNA quantification and fragmentation in sputum after inhalation of
recombinant human DNase)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 8 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2007:1330373 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 148:112291

TITLE: Identification of New Functional Inhibitors of Acid
Sphingomyelinase Using a Structure-Property-Activity
Relation Model

AUTHOR(S): Kornhuber, Johannes; Tripal, Philipp; Reichel, Martin;
Terfloth, Lothar; Bleich, Stefan; Wiltfang, Jens;
Gulbins, Erich

CORPORATE SOURCE: Department of Psychiatry and Psychotherapy, University
of Erlangen, Erlangen, D-91054, Germany

SOURCE: Journal of Medicinal Chemistry (2008), 51(2), 219-237
CODEN: JMCNAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

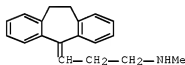
DOCUMENT TYPE: Journal

LANGUAGE: English

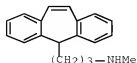
AB Some organic weak bases induce a detachment from inner lysosomal membranes and
subsequent inactivation of acid sphingomyelinase (ASM) and thus work as
functional ASM inhibitors. The aim of the present investigation was to
develop a structure-property-activity relation (SPAR) model in order to

specify the structural and physicochem. characteristics of probes capable of functionally inhibiting ASM. High pKa and high log P values are necessary but not sufficient preconditions for functional inhibition of ASM. The exptl. data supported the requirement of an addnl. factor, which is necessary for functional inhibition of ASM. This factor k is related to the steric hindrance of the most basic nitrogen atom and presumably modulates the free presentation of a protonated nitrogen atom at the inner lysosomal surface. During the course of the study, the authors characterized 26 new functional ASM inhibitors, including doxepine 63, fluoxetine 104, maprotiline 109, nortriptyline 114, paroxetine 118, sertraline 124, suloctidil 125, and terfenadine 127.

- CC 1-3 (Pharmacology)
- IT 54-30-8, Camylofin 58-40-2, Promazine 60-87-7, Promethazine 72-69-5, Nortriptyline 86-13-5, Benztropine 113-59-7, Chlorprothixene 129-03-3, Cyproheptadine 146-54-3, Triflupromazine 303-53-7, Cyclobenzaprine 314-03-4, Pimethixene 438-60-8, Protriptyline 911-45-5, Clomiphen 1668-19-5, Doxepine 1679-76-1, Drofenine 3703-76-2, Cloperastine 10262-69-8, Maprotiline 13042-18-7, Fendiline 50679-08-8, Terfenadine 54767-75-8, Suloctidil 54910-89-3, Fluoxetine 61869-08-7, Paroxetine 64706-54-3, Bepiridil 68844-77-9, Astemizole 79617-96-2, Sertraline 83891-03-6, Norfluoxetine 88150-42-9, Amlodipine
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (identification of new functional inhibitors of acid sphingomyelinase using a structure-property-activity relation model)
- IT 72-69-5, Nortriptyline 438-60-8, Protriptyline 1668-19-5, Doxepine 10262-69-8, Maprotiline
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (identification of new functional inhibitors of acid sphingomyelinase using a structure-property-activity relation model)
- RN 72-69-5 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



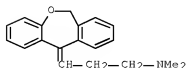
- RN 438-60-8 ZCAPLUS
- CN 5H-Dibenzo[a,d]cycloheptene-5-propanamine, N-methyl- (CA INDEX NAME)



10/524815

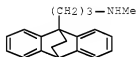
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 9 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 2007:1284150 ZCAPLUS Full-text

DOCUMENT NUMBER: 148:50999

TITLE: Ceramide in Pseudomonas aeruginosa infections

AUTHOR(S): Riethmuller, Joachim; Riehle, Andrea; Grassme, Heike; Gulbins, Erich

CORPORATE SOURCE: Children's Hospital, University of Tuebingen, Tuebingen, Germany

SOURCE: European Journal of Lipid Science and Technology (2007), 109(10), 998-1002

CODEN: EJLTFM; ISSN: 1438-7697

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Cystic fibrosis (CF), the most common autosomal recessive disorder, at least in western countries, is caused by mutations of the cystic fibrosis transmembranous conductance regulator (CFTR) mol. and affects approx. 80,000 patients in Europe and the USA. Most, if not all, CF patients develop a chronic pulmonary infection with Pseudomonas aeruginosa. At present it is unknown why CF patients are highly sensitive to P. aeruginosa infections, and most importantly, no curative treatment for CF is available. P. aeruginosa infection results in an activation of the enzyme acid sphingomyelinase which catalyzes the release of ceramide from sphingomyelin in the cell membrane. Ceramide forms large ceramide-enriched membrane domains that are required for internalization of bacteria, induction of cell death in infected cells and a controlled release of cytokines from infected cells. Ceramide-enriched membrane platforms seem to serve the reorganization of receptors and

intracellular signaling molcs. involved in the infection of mammalian cells with *P. aeruginosa*. The significance of the acid sphingomyelinase and ceramide for the infection of mammalian cells with *P. aeruginosa* was demonstrated on mice genetically deficient for the acid sphingomyelinase. Further studies with *N. gonorrhoeae*, *S. aureus* and rhinoviruses indicate that ceramide-enriched membrane domains are also important for the infection of mammalian cells with other bacterial and viral pathogens, suggesting a general role of these membrane domains in infectious biol.

CC 14-0 (Mammalian Pathological Biochemistry)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 10 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 2006:132218 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 144:290514

TITLE: Phospholipase A2 functions in *Pseudomonas aeruginosa*-induced apoptosis

AUTHOR(S): Kirschnek, Susanne; Gulbins, Erich

CORPORATE SOURCE: Department of Medical Microbiology, Technische Universität Munich, Munich, 81675, Germany

SOURCE: Infection and Immunity (2006), 74(2), 850-860

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Pseudomonas aeruginosa*, a gram-neg., facultative pathogen, causes severe and often even lethal infections in immunocompromised patients, as well as cystic fibrosis patients. We show here that a variety of *P. aeruginosa* strains activate phospholipase A2 (PLA2), cultured epithelial cells, and fibroblasts, resulting in increased intracellular and extracellular arachidonic acid release. The use of different PLA2 inhibitors revealed that *P. aeruginosa*-induced arachidonic acid release is mediated by activation of cytosolic PLA2 (cPLA2), whereas iPLA2 or sPLA2 do not seem to be involved in the response to *P. aeruginosa*. Likewise, the cPLA2-specific inhibitors MAFP and AACOCF3 prevented apoptosis of cultured epithelial cells upon *P. aeruginosa* infection, whereas inhibitors specific for iPLA2 or sPLA2 were without effect. The physiol. significance of these findings is indicated by an inhibition of apoptosis in tracheal epithelial cells upon in vivo infection with *P. aeruginosa*. The data indicate that arachidonic acid generation by activation of cPLA2 during *P. aeruginosa* infection plays an important role in the induction of host cell death.

CC 14-4 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 11 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 2005:1138242 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 144:184461

TITLE: High activity of acid sphingomyelinase in major depression

AUTHOR(S): Kornhuber, J.; Medlin, A.; Bleich, S.; Jendrossek, V.; Henkel, A. W.; Wiltfang, J.; Gulbins, E.

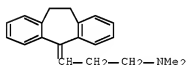
CORPORATE SOURCE: Department of Psychiatry, University of Erlangen, Germany

SOURCE: Journal of Neural Transmission (2005), 112(11), 1583-1590

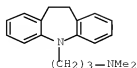
CODEN: JNTRF3; ISSN: 0300-9564

PUBLISHER: Springer Wien
 DOCUMENT TYPE: Journal
 LANGUAGE: English

- AB Acid sphingomyelinase (A-SMase) and its reaction product ceramide may play a role in the pathophysiol. of depressive disorders and in the therapeutic action of antidepressive drugs. In a prospective case-control study, A-SMase activity was measured in peripheral blood mononuclear cells of 17 patients with a major depressive episode who were free of antidepressant drug therapy for at least 10 days and 8 healthy volunteers. In the patient group, A-SMase activity was correlated to the score ($n = 17$, $r = 0.64$, $P = 0.005$). The patient group exhibited higher A-SMase activity compared to healthy volunteers ($T = 2.09$, $df = 21.33$, $P < 0.05$). In addition, we demonstrate that the antidepressants imipramine and amitriptyline induce a long-term reduction of the activity of A-SMase in cultured cells.
- CC 1-11 (Pharmacology)
- IT 50-48-6, Amitriptyline
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amitriptyline induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)
- IT 50-49-7, Imipramine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (imipramine induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)
- IT 50-48-6, Amitriptyline
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (amitriptyline induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



- IT 50-49-7, Imipramine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (imipramine induced long-term reduction of acid sphingomyelinase activity in peripheral blood mononuclear cell of healthy volunteer)
- RN 50-49-7 ZCAPLUS
- CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD
(9 CITINGS)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 12 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 2005:45517 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:294587
TITLE: Annexin II is a novel receptor for *Pseudomonas aeruginosa*
AUTHOR(S): Kirschnek, Susanne; Adams, Constantin; Gulbins, Erich
CORPORATE SOURCE: Department of Medical Microbiology, Technical
University Munich, Munich, 81675, Germany
SOURCE: Biochemical and Biophysical Research Communications
(2005), 327(3), 900-906
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infections with *P. aeruginosa* are critical in ventilated and poly-traumatized patients. Most important, these bacteria cause frequent and chronic pulmonary infections in patients with cystic fibrosis. Therefore, identification of mol. mechanisms that mediate the infection of mammalian cells with *P. aeruginosa* is urgently required. Here, we aimed to identify novel receptors that are involved in internalization of *P. aeruginosa* into mammalian epithelial cells. Employing SDS-PAGE purification and mass spectrometry we demonstrate that annexin II specifically binds to *P. aeruginosa*. The significance of the interaction of annexin II with *P. aeruginosa* for the infection of mammalian cells is indicated by the finding that neutralization of the ligands on *P. aeruginosa* by incubation of the bacteria with recombinant, soluble annexin II prevents internalization of *P. aeruginosa* into human epithelial cells.

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)
OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 13 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 14
ACCESSION NUMBER: 2003:155313 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:270184
TITLE: Host defense against *Pseudomonas aeruginosa* requires ceramide-rich membrane rafts
AUTHOR(S): Grassme, H.; Jendrossek, V.; Riehle, A.; von Kuerthy, G.; Berger, J.; Schwarz, H.; Weller, M.; Kolesnick, R.; Gulbins, E.
CORPORATE SOURCE: Department of Molecular Biology, University of Essen, Essen, Germany
SOURCE: Nature Medicine (New York, NY, United States) (2003), 9(3), 322-330
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB *Pseudomonas aeruginosa* infection is a serious complication in patients with cystic fibrosis and in immunocompromised individuals. Here the authors show that *P. aeruginosa* infection triggers activation of the acid sphingomyelinase and the release of ceramide in sphingolipid-rich rafts. Ceramide reorganizes these rafts into larger signaling platforms that are required to internalize *P. aeruginosa*, induce apoptosis and regulate the cytokine response in infected cells. Failure to generate ceramide-enriched membrane platforms in infected cells results in an unabated inflammatory response, massive release of interleukin (IL)-1 and septic death of mice. These findings show that ceramide-enriched membrane platforms are central to the host defense against this potentially lethal pathogen.

CC 15-8 (Immunchemistry)

Section cross-reference(s): 10

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: BSU (Biological study, unclassified); BIOL (Biological study) (clustering in mouse tracheal epithelium by *Pseudomonas aeruginosa* infection)

IT Cystic fibrosis

(host defense against *Pseudomonas aeruginosa* requires ceramide-rich membrane rafts in relation to)

OS.CITING REF COUNT: 147 THERE ARE 147 CAPLUS RECORDS THAT CITE THIS RECORD (147 CITINGS)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 14 OF 37 ZCAPLUS COPYRIGHT 2009 ACS ON STN DUPLICATE 15

ACCESSION NUMBER: 2001:240652 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 135:17827

TITLE: *Pseudomonas aeruginosa*-induced apoptosis involves mitochondria and stress-activated protein kinases
 AUTHOR(S): Jendrossek, Verena; Grassme, Heike; Mueller, Ilka; Lang, Florian; Gulbins, Erich

CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Tuebingen, 72076, Germany

SOURCE: Infection and Immunity (2001), 69(4), 2675-2683

CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Pseudomonas aeruginosa*, a gram-neg. facultative pathogen, causes severe infections in immunocompromised and cystic fibrosis patients. However, the mol. details of the interaction between *P. aeruginosa* and mammalian cells are still largely unknown. Here, infection of human conjunctiva epithelial Chang cells with the well-characterized *P. aeruginosa* strain PAO-I resulted in rapid induction of apoptosis. Apoptosis was mediated by mitochondrial alterations, in particular mitochondrial depolarization, synthesis of reactive oxygen intermediates, and release of cytochrome c, as well as an activation of Jun N-terminal kinases (JNK). Stimulation of these events was dependent on upregulation of CD95 on infected cells, and a deficiency of CD95 or the CD95 ligand prevented mitochondrial changes, JNK activation, and apoptosis upon infection. Further, efficient apoptosis of Chang epithelial cells required infection with live *P. aeruginosa*, adhesion but not invasion of the bacteria, and expression of the type III secretion system in PAO-I. The data indicate a type III secretion system-dependent, sequential activation of several signaling pathways by *P. aeruginosa* PAO-I, resulting in apoptosis of the infected cell.

10/524815

CC 14-3 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 10
IT Apoptosis
Cell adhesion
Cystic fibrosis
Immunodeficiency
Mitochondria
Pseudomonas aeruginosa
Signal transduction, biological
(Pseudomonas aeruginosa infection of epithelial cells induces apoptosis
via P. aeruginosa's type III secretion system which upregulates CD95
and stimulates JNK and mitochondrial alterations)
OS.CITING REF COUNT: 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS
RECORD (44 CITINGS)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 15 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 2001:20256 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 134:205873

TITLE: Invasion of human epithelial cells by Pseudomonas
aeruginosa involves Src-like tyrosine kinases p60Src
and p59Fyn

AUTHOR(S): Esen, Meral; Grassme, Heike; Riethmuller, Joachim;
Riehle, Andrea; Fassbender, Klaus; Gulbins, Erich
CORPORATE SOURCE: Department of Physiology, University of Tuebingen,
Tuebingen, 72076, Germany

SOURCE: Infection and Immunity (2001), 69(1), 281-287
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pseudomonas aeruginosa plays a major role in respiratory tract infections or
sepsis in patients with cystic fibrosis or upon suppression of the immune
system. Several P. aeruginosa strains have been shown to be internalized by
human epithelial cells; however, the mol. mechanisms of the invasion process
are poorly characterized. Here, the internalization of P. aeruginosa into
human epithelial cells resulted in and required activation of the Src-like
tyrosine kinases p59Fyn and p60Src and the consequent tyrosine phosphorylation
of several eukaryotic proteins. The significance of Src-like tyrosine kinase
activation is shown by an almost complete blockade of P. aeruginosa
internalization, but not adhesion, upon inhibition of Src-like tyrosine
kinases. Likewise, inhibition of P. aeruginosa binding to CFTR, which has
been shown to block P. aeruginosa internalization, prevents Src and Fyn
activation, supporting a pivotal role of Src-like tyrosine kinases for
invasion by P. aeruginosa.

CC 14-3 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 10

IT Cell adhesion

Cystic fibrosis

Pseudomonas aeruginosa

Sepsis

(invasion of human pulmonary epithelial cells by Pseudomonas aeruginosa
involves Src-like tyrosine kinases p60Src and p59Fyn)

IT CFTR (cystic fibrosis transmembrane
conductance regulator)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)

(invasion of human pulmonary epithelial cells by Pseudomonas aeruginosa
involves Src-like tyrosine kinases p60Src and p59Fyn)

10/524815

OS.CITING REF COUNT: 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS
RECORD (32 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 16 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 17

ACCESSION NUMBER: 2000:763385 ZCAPLUS Full-text

DOCUMENT NUMBER: 133:347707

TITLE: Physiology of apoptosis

AUTHOR(S): Gulbins, E.; Jekle, A.; Ferlinz, K.; Grassme, H.;
Lang, F.

CORPORATE SOURCE: Department of Physiology, University of Tuebingen,
Tuebingen, 72076, Germany

SOURCE: American Journal of Physiology (2000), 279(4, Pt. 2),
F605-F615

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 113 refs. Ion fluxes and volume changes of the whole cell as well as of organelles belong to the hallmarks of apoptosis; however, the mol. mechanism regulating these changes is only poorly characterized. Several ion channels in the plasma membrane, in particular the N-type K⁺ channel, the chloride channel cystic fibrosis conductance regulator, and an outward rectifying chloride channel, as well as the mitochondrial permeability transition pore, have been implicated to be involved in signal transduction cascades regulating apoptosis. Furthermore, Bcl-2-like proteins have been suggested to function, at least in part, as ion channels, because they display some homol. to bacterial pore-forming toxins. In contrast to the demonstration of the involvement of these different ion channels in apoptosis, the mol. consequences regulated by these ion channels, and finally triggering apoptosis, are almost completely unknown.

CC 13-0 (Mammalian Biochemistry)

OS.CITING REF COUNT: 68 THERE ARE 68 CAPLUS RECORDS THAT CITE THIS
RECORD (68 CITINGS)

REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L89 ANSWER 17 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 18

ACCESSION NUMBER: 2001:322701 ZCAPLUS Full-text

DOCUMENT NUMBER: 135:58810

TITLE: Tyrosine kinases open lymphocyte chloride channels

AUTHOR(S): Lepple-Wienhues, Albrecht; Szabo, Ildiko; Wieland,
Ulrich; Heil, Luzia; Gulbins, Erich; Lang, Florian

CORPORATE SOURCE: Department of Physiology I, University of Tubingen,
Tubingen, Germany

SOURCE: Cellular Physiology and Biochemistry (2000), 10(5-6),
307-312

CODEN: CEPBEW; ISSN: 1015-8987

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 41 refs. Osmotic swelling of lymphocytes opens outwardly rectifying Cl⁻ channels (ORCC) through the src-like kinase p56lck. The central role of this tyrosine protein kinase has been shown by genetic and pharmacol. manipulation of the enzyme. Furthermore, p56lck activates ORCC independently of cell volume increase. ORCC in lymphocytes and epithelial cells from cystic fibrosis (CF) patients are resistant to activation by cAMP. However, osmotic swelling as well as intracellular purified p56lck can

activate ORCC in CF lymphocytes. In non-CF lymphocytes ORCC is opened by either, intracellular cAMP, p56lck or by osmotic swelling. Osmotic activation of ORCC can be blocked by the tyrosine kinase inhibitor lavendustin in both cell types. Regulation of ORCC by p56lck thus represents an alternative pathway of stimulating membrane chloride conductance that is left functional in cystic fibrosis. In addition to osmoregulation these mechanisms could play a major role when cells actively change their volume, i.e. during proliferation and apoptosis. Activation of the tyrosine kinase p56lck is an important regulatory step for opening of chloride channels in lymphocytes.

CC 13-0 (Mammalian Biochemistry)
Section cross-reference(s): 14

ST review lck tyrosine kinase chloride channel osmotic apoptosis lymphocyte;
cystic fibrosis chloride channel tyrosine kinase review

IT Cystic fibrosis
(tyrosine kinases, cAMP and osmotic swelling in regulation of
lymphocyte chloride channels in relation to)

OS.CITING REF COUNT: 30 THERE ARE 30 CAPLUS RECORDS THAT CITE THIS
RECORD (30 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 18 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:827242 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 151:108500

TITLE: Pharmaceutical composition for prophylaxis and/or
symptomatic treatment of cystic fibrosis with
antidepressants

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Cynad GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
PRIORITY APPLN. INFO.:			DE 2007-102007063535A	20071221

AB The invention relates to a pharmaceutical compound for the prophylaxis and/or symptomatic treatment of cystic fibrosis, particularly for the prophylaxis and/or treatment of infections and/or infection illnesses manifesting with cystic fibrosis, having at least one anti-depressive and preferable at least one dispersion agent and/or at least one pharmaceutically tolerated carrier material. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus Cfr-knockout mice and wild-type mice were

treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration

IC ICM A61K

CC 63-6 (Pharmaceuticals)

ST Section cross-reference(s): 1, 14

IT cystic fibrosis antidepressant inhalant

5-HT reuptake inhibitors

Antidepressants

Burkholderia cepacia

Cystic fibrosis

Dopamine reuptake inhibitors

Haemophilus influenzae

Inhalation drug delivery systems

Lung

Noradrenaline reuptake inhibitors

Parenteral drug delivery systems

Pharmaceutical solutions

Prophylaxis

Pseudomonas aeruginosa

Staphylococcus aureus

Therapy

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT Antibodies and Immunoglobulins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 111-57-9, Ceramid 9031-54-3, Sphingomyelinase

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenalin 51-61-6, Dopamine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline

50-49-7, Imipramine 58-40-2, Promazine 72-69-5,

Nortriptyline 86-13-5, Benztropine 113-45-1, Methylphenidate 129-03-3, Cyproheptadine 155-09-9, Tranylcypromine 256-96-2D,

5H-Dibenz[b,f]azepine, derivative 303-49-1 303-53-7,

Cyclobenzaprine 315-72-0 494-19-9,

10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine 911-45-5, Clomiphen 1668-19-5, Doxepine 4317-14-0,

Amitriptyline oxide 4498-32-2, Dibenzepine 6621-47-2,

Perhexiline 10262-69-8, Maprotiline 19794-93-5, Trazodon 23047-25-8, Lofepramine 24219-97-4, Mianserin 24526-64-5, Nomifensin 32359-34-5, Medifoxamine 34911-55-2, Bupropion 46817-91-8, Viloxazine 54739-18-3, Fluvoxamine 57574-09-1,

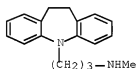
Amineptine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71320-77-9, Moclobemide 71620-89-8, Reboxetine 72797-41-2, Tianeptine 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 92623-85-3, Milnacipran 93413-69-5, Venlafaxin 116539-59-4, Duloxetine 128196-01-0, Escitalopram

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

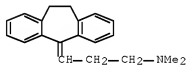
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

10/524815

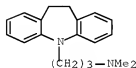
IT 50-47-5, Desipramine 50-48-6, Amitriptyline
 50-49-7, Imipramine 72-69-5, Nortriptyline
 303-49-1 315-72-0 739-71-9, Trimipramine
 1668-19-5, Doxepine 4498-32-2, Dibenzepine
 10262-69-8, Maprotiline 23047-25-8, Lofepramine
 24219-97-4, Mianserin 57574-09-1, Amineptine
 72797-41-2, Tianeptine 85650-52-8, Mirtazapine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of
 cystic fibrosis with antidepressants)
 RN 50-47-5 ZCAPLUS
 CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX
 NAME)



RN 50-48-6 ZCAPLUS
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-
 dimethyl- (CA INDEX NAME)

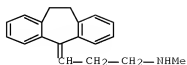


RN 50-49-7 ZCAPLUS
 CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA
 INDEX NAME)



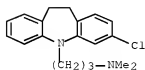
RN 72-69-5 ZCAPLUS
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-
 methyl- (CA INDEX NAME)

10/524815



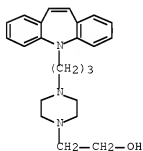
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl-
(CA INDEX NAME)



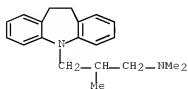
RN 315-72-0 ZCAPLUS

CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX
NAME)



RN 739-71-9 ZCAPLUS

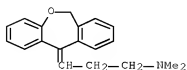
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl-
(CA INDEX NAME)



RN 1668-19-5 ZCAPLUS

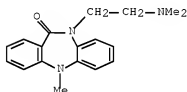
10/524815

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



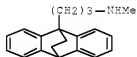
RN 4498-32-2 ZCAPLUS

CN 11H-Dibenzo[b,e][1,4]diazepin-11-one,
10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



RN 10262-69-8 ZCAPLUS

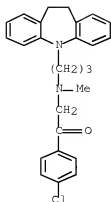
CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



RN 23047-25-8 ZCAPLUS

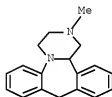
CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl)methylamino]- (CA INDEX NAME)

10/524815



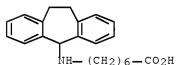
RN 24219-97-4 ZCAPLUS

CN Dibenzo[c,f]pyrazino[1,2-a]azepine, 1,2,3,4,10,14b-hexahydro-2-methyl-
(CA INDEX NAME)



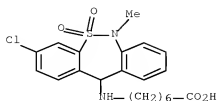
RN 57574-09-1 ZCAPLUS

CN Heptanoic acid, 7-[(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)amino]-
(CA INDEX NAME)

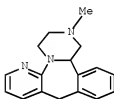


RN 72797-41-2 ZCAPLUS

CN Heptanoic acid, 7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[c,f][1,2]thiazepin-11-yl)amino]- (CA INDEX NAME)



RN 85650-52-8 ZCAPLUS
 CN Pyrazino[2,1-a]pyrido[2,3-c][1,2]benzazepine,
 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L89 ANSWER 19 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2009:891218 ZCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 151:120391
 TITLE: Cystic fibrosis - pathophysiological concepts
 AUTHOR(S): Becker, Katrin Anne; Riethmueller, Joachim; Doering,
 Gerd; Gulbins, Erich
 CORPORATE SOURCE: Institut fuer Molekularbiologie, Universitaetsklinikum
 Essen, Universitaet Duisburg-Essen, Essen, Germany
 SOURCE: BIOSpektrum (2009), 15(4), 383-385
 CODEN: BOSPF; ISSN: 0947-0867
 PUBLISHER: Spektrum Akademischer Verlag GmbH
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: German
 AB A review. Cystic fibrosis patients very often suffer from chronic pulmonary
 infections, in particular with *Pseudomonas aeruginosa*. The mol. mechanisms of
 the very high infection susceptibility of these patients are presently
 unknown.
 CC 14-0 (Mammalian Pathological Biochemistry)
 ST review cystic fibrosis ceramide pathophysiol chronic infection
 IT Lung disease
 (chronic, infection; cystic fibrosis, ceramides in
 pathophysiol., and chronic infections)
 IT Cystic fibrosis
 Human
 (cystic fibrosis, ceramides in pathophysiol., and
 chronic infections)
 IT Ceramides
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (cystic fibrosis, ceramides in pathophysiol., and
 chronic infections)
 REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

L89 ANSWER 20 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:177956 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:193037

TITLE: Use of inhibitors of acid sphingomyelinase and of acid sphingomyelinase reaction products for the prophylaxis and treatment of infectious diseases

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 10 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10239531	A1	20040304	DE 2002-10239531	20020823
CA 2497582	A1	20040304	CA 2003-2497582	20030821
WO 2004017949	A2	20040304	WO 2003-EP9254	20030821
WO 2004017949	A3	20040429		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003255468	A1	20040311	AU 2003-255468	20030821
EP 1531826	A2	20050525	EP 2003-792402	20030821
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
CN 1688316	A	20051026	CN 2003-824405	20030821
CN 100502875	C	20090624		
JP 2006505527	T	20060216	JP 2004-530234	20030821
US 20050209219	A1	20050922	US 2005-524815	20050218
PRIORITY APPLN. INFO.:			DE 2002-10239531	A 20020823
			WO 2003-EP9254	W 20030821

AB The invention concerns the use of inhibitors of acid sphingomyelinase and/or of inhibitors of products (especially ceramide) catalyzed by reaction of this enzyme for prophylaxis and/or therapy of infectious diseases. Inhibitors include antibodies, especially neutralizing antibodies, and/or antidepressants, especially tricyclic and/or tetracyclic antidepressants.

ICM A61K039-395

CC 1-5 (Pharmacology)

Section cross-reference(s): 15

IT 50-48-6, Amitriptyline 50-49-7, Imipramine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors of acid sphingomyelinase and of acid sphingomyelinase reaction products for prophylaxis and treatment of infectious diseases)

IT 50-48-6, Amitriptyline 50-49-7, Imipramine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

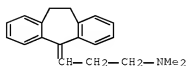
(inhibitors of acid sphingomyelinase and of acid sphingomyelinase

10/524815

reaction products for prophylaxis and treatment of infectious diseases)

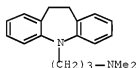
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



RN 50-49-7 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



L89 ANSWER 21 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:171714 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:210564

TITLE: Detecting and influencing the expression or function of CD95/CD95L in infections

INVENTOR(S): Lang, Florian; Gulbins, Erich

PATENT ASSIGNEE(S): Germany

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017950	A2	20020307	WO 2001-EP9889	20010828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042853	A1	20020425	DE 2000-10042853	20000830
AU 2002012170	A	20020313	AU 2002-12170	20010828

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PRIORITY APPLN. INFO.:

DE 2000-10042853 A 20000830
WO 2001-EP9889 W 20010828

AB The invention discloses the use of a substance for detecting CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, in order to identify susceptibility to diseases that are related to an infection. The invention also discloses the use of an active substance for preventing and treating infections, in particular, bacterial infections, in which the active substance influences the expression and/or function of CD95 and/or CD95L, or members of the signal transduction cascade of CD95 and/or CD95L, thereby inducing apoptosis in the infected cells.

IC ICM A61K038-00

CC 1-7 (Pharmacology)

Section cross-reference(s): 9, 15

IT CFTR (cystic fibrosis transmembrane conductance regulator)

Fas antigen

Fas ligand

RL: BSU (Biological study, unclassified); BIOL (Biological study) (CD95/CD95L detection and modulation in infections)

L89 ANSWER 22 OF 37 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:623548 ZCAPLUS Full-text

DOCUMENT NUMBER: 133:187991

TITLE: Use of ceramides in the treatment of cystic fibrosis and other diseases associated with impaired membrane transport regulation

INVENTOR(S): Lang, Florian; Gulbins, Erich; Lepple-Wienhues, Albrecht

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 8 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19909115	A1	20000907	DE 1999-19909115	19990303
CA 2365290	A1	20000908	CA 2000-2365290	20000229
WO 2000051578	A2	20000908	WO 2000-EP1682	20000229
WO 2000051578	A3	20010104		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156854	A2	20011128	EP 2000-909267	20000229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

DE 1999-19909115 A 19990303
WO 2000-EP1682 W 20000229

AB The invention provides the use of ceramides (especially C2 and/or C6 ceramide), and/or substances which contain ceramides as components, for the treatment of cystic fibrosis. The invention also provides the use of the above-mentioned substances for the treatment of diseases which are associated with impaired regulation of membrane transport processes.

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IC ICM A61K031-16
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
ST C2 C6 ceramide cystic fibrosis treatment; membrane transport
regulation disease treatment ceramide
IT Biological transport
Cystic fibrosis
Drug delivery systems
Membrane, biological
T cell (lymphocyte)
(ceramides for treatment of cystic fibrosis and
other diseases associated with impaired membrane transport regulation)
IT Ceramides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(ceramides for treatment of cystic fibrosis and
other diseases associated with impaired membrane transport regulation)
IT Chloride channel
Ion channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(ceramides for treatment of cystic fibrosis and
other diseases associated with impaired membrane transport regulation)
IT 114051-78-4
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(ceramides for treatment of cystic fibrosis and
other diseases associated with impaired membrane transport regulation)
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L89 ANSWER 23 OF 37 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2009022109 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 19022708
TITLE: Highlights of a workshop to discuss targeting inflammation
in cystic fibrosis.
AUTHOR: Banner Katharine H; De Jonge Hugo; Elborn Stuart; Growcott
Ellena; Gulbins Erich; Konstan Mike; Moss Rick; Poll
Chris; Randell Scott H; Rossi Adriano G; Thomas Lorraine;
Waltz David
CORPORATE SOURCE: Novartis Institutes for Biomedical Research, Wimblehurst
Road, Horsham, West Sussex, RH12 5AB, UK..
kathy.banner@novartis.com
SOURCE: Journal of cystic fibrosis : official journal of the
European Cystic Fibrosis Society, (2009 Jan) Vol. 8, No. 1,
pp. 1-8. Electronic Publication: 2008-11-20. Ref: 78
Journal code: 101128966. ISSN: 1569-1993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200903

10/524815

ENTRY DATE: Entered STN: 2 Jan 2009
Last Updated on STN: 11 Mar 2009
Entered Medline: 10 Mar 2009

ABSTRACT:

A workshop to discuss anti-inflammatory approaches in the treatment of CF was held at Novartis Institutes for Biomedical Research (NIBR, Horsham, UK) in March 2008. Key opinion leaders in the field (Hugo De Jonge, Stuart Elborn, Erich Gulbins, Mike Konstan, Rick Moss, Scott Randell and Adriano Rossi), and NIBR scientists were brought together to collectively address three main aims: (i) to identify anti-inflammatory targets in CF, (ii) to evaluate the pros and cons of targeting specific cell types and (iii) to discuss model systems to profile potential therapeutic agents. The highlights of the workshop are captured in this review.

CONTROLLED TERM: Animals
*Anti-Inflammatory Agents: TU, therapeutic use
Cystic Fibrosis: CO, complications
*Cystic Fibrosis: DT, drug therapy
*Cystic Fibrosis: PA, pathology
Education
Epithelial Cells: ME, metabolism
Humans
Inflammation: CO, complications
*Inflammation: DT, drug therapy
*Inflammation: PA, pathology
Lymphocytes: ME, metabolism
Models, Biological
Neutrophils: ME, metabolism
Research Design

CHEMICAL NAME: 0 (Anti-Inflammatory Agents)

L89 ANSWER 24 OF 37 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 2000420364 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10930579
TITLE: Acid sphingomyelinase is involved in CEACAM
receptor-mediated phagocytosis of Neisseria gonorrhoeae.
AUTHOR: Hauck C R; Grassme H; Bock J; Jendrosseck V; Ferlinz K;
Meyer T F; Gulbins E
CORPORATE SOURCE: Department of Physiology, University of Tübingen, Germany.
SOURCE: FEBS letters, (2000 Aug 4) Vol. 478, No. 3, pp. 260-6.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 15 Sep 2000
Last Updated on STN: 22 Sep 2000
Entered Medline: 7 Sep 2000

ABSTRACT:

The interaction with human phagocytes is a hallmark of symptomatic Neisseria gonorrhoeae infections. Gonococcal outer membrane proteins of the Opa family induce the opsonin-independent uptake of the bacteria that relies on CEACAM receptors and an active signaling machinery of the phagocyte. Here, we show that CEACAM receptor-mediated phagocytosis of Opa(52)-expressing N. gonorrhoeae into human cells results in a rapid activation of the acid sphingomyelinase. Inhibition of this enzyme by imipramine or SR33557 abolishes opsonin-independent internalization without affecting bacterial adherence. Reconstitution of ceramide, the product of acid sphingomyelinase activity, in imipramine- or SR33557-treated cells restores internalization of the

bacteria. Furthermore, we demonstrate that CEACAM receptor-initiated stimulation of other signalling molecules, in particular Src-like tyrosine kinases and Jun N-terminal kinases, requires acid sphingomyelinase. These studies provide evidence for a crucial role of the acid sphingomyelinase for CEACAM receptor-initiated signalling events and internalization of Opa(52)-expressing *N. gonorrhoeae* into human neutrophils.

CONTROLLED TERM: Antigens, Bacterial: ME, metabolism
 Bacterial Adhesion: DE, drug effects
 Bacterial Outer Membrane Proteins: ME, metabolism
 *Carcinoembryonic Antigen: ME, metabolism
 Cell Line
 Ceramides: PD, pharmacology
 Enzyme Activation
 Epithelial Cells: CY, cytology
 Epithelial Cells: DE, drug effects
 Epithelial Cells: EN, enzymology
 Epithelial Cells: MI, microbiology
 Humans
 Imipramine: FD, pharmacology
 Indolizines: PD, pharmacology
 Mitogen-Activated Protein Kinase 8
 Mitogen-Activated Protein Kinases: ME, metabolism
 Neisseria gonorrhoeae: IM, immunology
 *Neisseria gonorrhoeae: ME, metabolism
 Phagocytes: DE, drug effects
 *Phagocytes: EN, enzymology
 *Phagocytes: IM, immunology
 Phagocytes: MI, microbiology
 *Phagocytosis
 Phagocytosis: DE, drug effects
 Phenethylamines: PD, pharmacology
 Proto-Oncogene Proteins pp60(c-src): AI, antagonists & inhibitors
 Proto-Oncogene Proteins pp60(c-src): ME, metabolism
 *Receptors, Cell Surface: ME, metabolism
 Signal Transduction: DE, drug effects
 Sphingomyelin Phosphodiesterase: AI, antagonists & inhibitors
 *Sphingomyelin Phosphodiesterase: ME, metabolism
 114432-13-2 (fantofarone); 50-49-7 (Imipramine)
 0 (Antigens, Bacterial); 0 (Bacterial Outer Membrane Proteins); 0 (Carcinoembryonic Antigen); 0 (Ceramides); 0 (Indolizines); 0 (Phenethylamines); 0 (Receptors, Cell Surface); 0 (opacity proteins); EC 2.7.1.112 (Proto-Oncogene Proteins pp60(c-src)); EC 2.7.1.37 (Mitogen-Activated Protein Kinase 8); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase)

L89 ANSWER 25 OF 37 MEDLINE on STN
 ACCESSION NUMBER: 2009071090 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 19068098
 TITLE: Cystic fibrosis and innate immunity: how chloride channel mutations provoke lung disease.
 AUTHOR: Doring Gerd; Gulbins Erich
 CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene, Wilhelmstrasse 31, 72074 Tübingen, Germany..
 gerd.doering@med.uni-tuebingen.de
 SOURCE: Cellular microbiology, (2009 Feb) Vol. 11, No. 2, pp. 208-16. Electronic Publication: 2008-12-02. Ref: 60

Journal code: 100883691. E-ISSN: 1462-5822.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200902
 ENTRY DATE: Entered STN: 16 Jan 2009
 Last Updated on STN: 1 Mar 2009
 Entered Medline: 27 Feb 2009

ABSTRACT:

Innate immunity is essential for prevention of infection in vertebrates and plants and dysfunction of single components of innate immunity may provoke severe disease. Here we describe how mutations in the cystic fibrosis transmembrane conductance regulator gene dysregulate a variety of components of the innate immune system in individuals suffering from the hereditary disease cystic fibrosis. In the airways of these individuals, functions of the mucociliary clearance system, cationic antimicrobial (poly)peptides and neutrophils and macrophages are impaired and inflammatory signal transduction pathways exaggerated. Consequently, chronic airway colonization with opportunistic bacterial pathogens develops and leads to life-threatening lung disease.

CONTROLLED TERM: Animals
 *Chloride Channels: GE, genetics
 *Chloride Channels: IM, immunology
 *Cystic Fibrosis: PA, pathology
 Humans
 *Immunity, Innate
 *Mutation
 CHEMICAL NAME: 0 (Chloride Channels)

L89 ANSWER 26 OF 37 MEDLINE on STN
 ACCESSION NUMBER: 2009476152 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 19590194
 TITLE: Therapeutic efficacy and safety of amitriptyline in patients with cystic fibrosis.
 AUTHOR: Riethmuller Joachim; Anthonysamy Janina; Serra Emilio; Schwab Matthias; Doring Gerd; Gulbins Erich
 CORPORATE SOURCE: Department of Paediatrics, University Hospital Tuebingen, Tuebingen, Germany.. joachim.riethmueller@med.uni-tuebingen.de
 SOURCE: Cellular physiology and biochemistry : international journal of experimental cellular physiology, biochemistry, and pharmacology, (2009) Vol. 24, No. 1-2, pp. 65-72. Electronic Publication: 2009-07-01. Journal code: 9113221. E-ISSN: 1421-9778.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: (CLINICAL TRIAL, PHASE II)
 Journal; Article; (JOURNAL ARTICLE)
 (RANDOMIZED CONTROLLED TRIAL)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (CLINICAL TRIAL)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200910
 ENTRY DATE: Entered STN: 11 Jul 2009
 Last Updated on STN: 6 Oct 2009
 Entered Medline: 5 Oct 2009

ABSTRACT:

Amitriptyline, a blocker of acid sphingomyelinase and acid ceramidase,

significantly reduces *Pseudomonas aeruginosa* lung infection in cystic fibrosis (CF) mice with concurrent increase of survival. Our aim was to establish whether amitriptyline is safe and effective in the treatment of CF patients. In a randomised, double-blinded, placebo-controlled, cross-over pilot study, 4 adult CF patients received 37.5 mg of amitriptyline or placebo twice daily for 14 days. Subsequently in a phase II study 19 adult CF patients were randomly allocated to three treatment groups receiving amitriptyline once daily for 28 days at doses of 25 mg (n=7), 50 mg (n=8), or 75 mg (n=8) or placebo (n=13). The primary outcome was the difference of forced expiratory volume in 1 sec (FEV(1)) at day 14 between amitriptyline and placebo. Primary endpoint measures improved significantly in three of four patients in the pilot study after amitriptyline treatment vs placebo (relative FEV(1): 14.7+/-5%; p = 0.006) and in the 25 mg treatment group of the phase II study (relative FEV(1): 4.0+/-7%; p = 0.048). Amitriptyline was well tolerated in both studies and 96% of the patients completed the studies. Amitriptyline as a novel therapeutic option in patients with CF is safe and seems to be efficacious.

2009 S. Karger AG, Basel.

CONTROLLED TERM: Check Tags: Female; Male
Adult
Amitriptyline: AE, adverse effects
*Amitriptyline: TU, therapeutic use
Anti-Bacterial Agents: AE, adverse effects
*Anti-Bacterial Agents: TU, therapeutic use
*Bacterial Infections: DT, drug therapy
*Cystic Fibrosis: DT, drug therapy
Enzyme Inhibitors: AE, adverse effects
*Enzyme Inhibitors: TU, therapeutic use
Forced Expiratory Volume
Humans
Pseudomonas Infections: DT, drug therapy
Pseudomonas Infections: ET, etiology
Treatment Outcome
CAS REGISTRY NO.: 50-48-6 (Amitriptyline)
CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Enzyme Inhibitors)

L89 ANSWER 27 OF 37 MEDLINE on STN
ACCESSION NUMBER: 2008548021 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 18751925
TITLE: Ceramide-enriched membrane domains in infectious biology and development.
AUTHOR: Becker Katrin Anne; Gellhaus Alexandra; Winterhager Elke; Gulbins Erich
CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany.
SOURCE: Sub-cellular biochemistry, (2008) Vol. 49, pp. 523-38.
Ref: 79
Journal code: 0316571. ISSN: 0306-0225.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200812
ENTRY DATE: Entered STN: 29 Aug 2008
Last Updated on STN: 2 Jan 2009
Entered Medline: 24 Dec 2008
ABSTRACT:

Ceramide has been shown to be critically involved in multiple biological

processes, for instance induction of apoptosis after ligation of death receptors or application of gamma-irradiation or UV-A light, respectively, regulation of cell differentiation, control of tumor cell growth, infection of mammalian cells with pathogenic bacteria and viruses or the control of embryo and organ development to name a few examples. Ceramide molecules form distinct large domains in the cell membrane, which may serve to re-organize cellular receptors and signalling molecules. Thus, in many conditions, ceramide may be involved in the spatial and temporal organisation of specific signalling pathways explaining the pleiotrophic effects of this lipid. Here, we focus on the role of ceramide and ceramide-enriched membrane domains, respectively, in bacterial infections, in particular of the lung, and sepsis. We describe the role of ceramide for infections with *Neisseriae gonorrhoeae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Finally, we discuss newly emerging aspects of the cellular function of ceramide, i.e. its role in germ line and embryo development.

CONTROLLED TERM: Check Tags: Female; Male
 Animals
 Apoptosis: DE, drug effects
 *Bacterial Infections: PP, physiopathology
 *Cell Membrane: PH, physiology
 *Ceramides: PH, physiology
 Cystic Fibrosis: PP, physiopathology
 Embryo Implantation: PH, physiology
 *Embryonic Development: PH, physiology
 Germ Cells: GD, growth & development
 Gonorrhea: EN, enzymology
 Gonorrhea: ET, etiology
 Humans
 Parasitic Diseases: PP, physiopathology
 Pseudomonas Infections: ET, etiology
 Sepsis: EN, enzymology
 Sphingomyelin Phosphodiesterase: ME, metabolism
 Staphylococcal Infections: ET, etiology
 Virus Diseases: PP, physiopathology
 CHEMICAL NAME: 0 (Ceramides); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase)

L89 ANSWER 28 OF 37 MEDLINE on STN
 ACCESSION NUMBER: 2005353059 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15888438
 TITLE: Rhinoviruses infect human epithelial cells via ceramide-enriched membrane platforms.
 AUTHOR: Grassme Heike; Riehle Andrea; Wilker Barbara; Gulbins Erich
 CORPORATE SOURCE: Department of Molecular Biology, University of Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany.
 SOURCE: The Journal of biological chemistry, (2005 Jul 15) Vol. 280, No. 28, pp. 26256-62. Electronic Publication: 2005-05-10.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200509
 ENTRY DATE: Entered STN: 12 Jul 2005
 Last Updated on STN: 13 Sep 2005
 Entered Medline: 12 Sep 2005

ABSTRACT:
 The cell membrane contains very small distinct membrane domains enriched of

sphingomyelin and cholesterol that are named rafts. We have shown that the formation of ceramide via activation of the acid sphingomyelinase transforms rafts into ceramide-enriched membrane platforms. These platforms are required for infection of mammalian cells with *Pseudomonas aeruginosa*, *Staphylococcus aureus*, or *Neisseriae gonorrhoeae*. In the present study we determined whether the acid sphingomyelinase, ceramide, and ceramide-enriched membrane platforms are also involved in the infection of human cells with pathogenic rhinoviruses. We demonstrate that infection of human epithelial cells with several rhinovirus strains triggers a rapid activation of the acid sphingomyelinase correlating with microtubules- and microfilament-mediated translocation of the enzyme from an intracellular compartment onto the extracellular leaflet of the cell membrane. The activity of the acid sphingomyelinase results in the formation of ceramide in the cell membrane and, finally, large ceramide-enriched membrane platforms. Rhinoviruses colocalize with ceramide-enriched membrane platforms during the infection. The significance of ceramide-enriched membrane platforms for rhinoviral uptake is demonstrated by the finding that genetic deficiency or pharmacological inhibition of the acid sphingomyelinase prevented infection of human epithelial cells by rhinoviruses. The data identify the acid sphingomyelinase and ceramide as key molecules for the infection of human cells with rhinoviruses.

CONTROLLED TERM:

Adrenergic Uptake Inhibitors: PD, pharmacology

Amitriptyline: PD, pharmacology

Annexins: PD, pharmacology

Cell Line

*Cell Membrane: ME, metabolism

Ceramides: ME, metabolism

*Ceramides: PD, pharmacology

Diacylglycerol Kinase: ME, metabolism

Enzyme Activation

Enzyme Inhibitors: PD, pharmacology

*Epithelial Cells: ME, metabolism

Epithelial Cells: VI, virology

Fibroblasts: ME, metabolism

Hela Cells

Humans

Imipramine: PD, pharmacology

Membrane Microdomains: CH, chemistry

Microfilaments: ME, metabolism

Microscopy, Confocal

Microscopy, Fluorescence

Microtubules: ME, metabolism

Neisseria gonorrhoeae: ME, metabolism

Protein Transport

Pseudomonas aeruginosa: ME, metabolism

*Rhinovirus: ME, metabolism

Sphingomyelin Phosphodiesterase: CH, chemistry

Sphingomyelin Phosphodiesterase: GE, genetics

Sphingomyelins: CH, chemistry

Sphingomyelins: ME, metabolism

Staphylococcus aureus: ME, metabolism

Time Factors

CAS REGISTRY NO.: 50-48-6 (Amitriptyline); 50-49-7 (Imipramine)

CHEMICAL NAME: 0 (Adrenergic Uptake Inhibitors); 0 (Annexins); 0 (Ceramides); 0 (Enzyme Inhibitors); 0 (Sphingomyelins); EC 2.7.1.107 (Diacylglycerol Kinase); EC 3.1.4.- (acid sphingomyelinase-1); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase)

L89 ANSWER 29 OF 37 MEDLINE on STN

ACCESSION NUMBER: 1999218554 MEDLINE [Full-text](#)

10/524815

DOCUMENT NUMBER: PubMed ID: 10200443
TITLE: Fas/CD95/Apo-I activates the acidic sphingomyelinase via caspases.
AUTHOR: Brenner B; Ferlinz K; Grassme H; Weller M; Koppenhoefer U; Dichgans J; Sandhoff K; Lang F; Gulbins E
CORPORATE SOURCE: Department of Physiology, University of Tuebingen, Gmelinstrasse 5, 72076 Tuebingen, Germany.
SOURCE: Cell death and differentiation, (1998 Jan) Vol. 5, No. 1, pp. 29-37.
Journal code: 9437445. ISSN: 1350-9047.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 17 May 1999
Last Updated on STN: 17 May 1999
Entered Medline: 30 Apr 1999

ABSTRACT:

Fas/CD95/Apo-I has been shown to stimulate a variety of molecules including several members of the caspase family and the acidic sphingomyelinase (Martin and Green 1995; Gulbins et al, 1995). Here, we demonstrate that Fas receptor-triggered activation of the acidic sphingomyelinase, consumption of sphingomyelin, release of ceramide, and subsequent activation of JNK and p38-K are regulated by caspases. Inhibition of caspases by Ac-YVAD-chloromethylketone or transient CrmA transfection prevented stimulation of acidic sphingomyelinase, release of ceramide and activation of JNK and p38-K upon Fas-receptor crosslinking. Likewise, Fas triggered apoptosis was almost completely blocked by Ac-YVAD-chloromethylketone or CrmA mediated inhibition of caspases. The results suggest a new signalling cascade from the Fas receptor via caspases to acidic sphingomyelinase, ceramide and JNK/p38-K.

CONTROLLED TERM: Acids: ME, metabolism
Adrenergic Uptake Inhibitors: PD, pharmacology
Amino Acid Chloromethyl Ketones: PD, pharmacology
*Antigens, CD95: ME, metabolism
Apoptosis: DE, drug effects
*Apoptosis: PH, physiology
Calcium-Calmodulin-Dependent Protein Kinases: ME, metabolism
*Caspases: ME, metabolism
Ceramide: ME, metabolism
Cysteine Proteinase Inhibitors: GE, genetics
Cysteine Proteinase Inhibitors: PD, pharmacology
Diglycerides: ME, metabolism
Gene Expression Regulation, Enzymologic
Humans
Imipramine: PD, pharmacology
*Jurkat Cells: CY, cytology
Jurkat Cells: EN, enzymology
*Mitogen-Activated Protein Kinases
Serpins: GE, genetics
Signal Transduction: PH, physiology
*Sphingomyelin Phosphodiesterase: ME, metabolism
T-Lymphocytes: CY, cytology
T-Lymphocytes: EN, enzymology
Transfection
*Viral Proteins
p38 Mitogen-Activated Protein Kinases
CAS REGISTRY NO.: 50-49-7 (Imipramine); 96282-35-8

CHEMICAL NAME: (interleukin-1beta-converting enzyme inhibitor)
 0 (Acids); 0 (Adrenergic Uptake Inhibitors); 0 (Amino Acid Chloromethyl Ketones); 0 (Antigens, CD95); 0 (Ceramides); 0 (Cysteine Proteinase Inhibitors); 0 (Diglycerides); 0 (N-acetyl-tyrosyl-valyl-alanyl-aspartyl chloromethyl ketone); 0 (Serpins); 0 (Viral Proteins); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p38 Mitogen-Activated Protein Kinases); EC 2.7.11.17 (Calcium-Calmodulin-Dependent Protein Kinases); EC 3.1.4.12 (Sphingomyelin Phosphodiesterase); EC 3.4.22.- (Caspases)

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ACCESSION NUMBER: 2007054516 EMBASE Full-text
 TITLE: The cold case: Are rhinoviruses perfectly adapted pathogens?
 AUTHOR: Dreschers, S. (correspondence); Dumitru, C.A.; Adams, C.; Gulbins, E.
 CORPORATE SOURCE: Dept. of Molecular Biology, University of Duisburg-Essen, Hufelandstr. 55, 45122 Essen, Germany. stephan.dreschers@uni-essen.de
 SOURCE: Cellular and Molecular Life Sciences, (Jan 2007) Vol. 64, No. 2, pp. 181-191.
 Refs: 88
 ISSN: 1420-682X; E-ISSN: 1569-1632 CODEN: CMLSFI
 COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 011 Otorhinolaryngology
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 14 Feb 2007
 Last Updated on STN: 14 Feb 2007

ABSTRACT: Rhinoviruses, which cause common cold, belong to the Picornaviridae family, small non-enveloped viruses (diameter 15-30 nm) containing a single-stranded RNA genome (about 7 kb). Over 100 different rhinoviral serotypes have been identified thus far, establishing rhinoviruses as the most diverse group of Picomaviridae. Based on receptor binding properties, rhinoviruses are divided into two classes: the major group binding to intracellular adhesion molecule-1 and the minor group binding to the very low density lipoprotein receptors. Interactions between virus and the receptor molecules cause a conformational change in the capsid, which is a prerequisite for viral uptake. Rhinoviruses trigger a chemokine response upon infection that may lead to exacerbation of the symptoms of common cold, i.e. asthma and inflammation. The following review aims to summarize the knowledge about rhinoviral infections and discusses therapeutical approaches against this almost perfectly adapted pathogen. .COPYRG. Birkhauser Verlag, 2007.

CONTROLLED TERM: Medical Descriptors:
 absence of side effects: SI, side effect
 asthma
 chronic obstructive lung disease
 clinical feature
 *common cold: DI, drug therapy
 *common cold: ET, etiology
 disease exacerbation

drug megadose
 electron microscopy
 human
 internalization
 lipid composition
 nonhuman
 nose congestion: SI, side effect
 nose injury: SI, side effect
 open reading frame
 protein family
 protein structure
 review
 *Rhinovirus
 signal transduction
 upper respiratory tract infection: ET, etiology
 virion
 virus capsid
 virus classification
 virus detection
 virus envelope
 virus identification
 virus morphogenesis
 virus morphology
 virus strain
 virus transmission
 virus virulence
 X ray crystallography

CONTROLLED TERM:

Drug Descriptors:
 amitriptyline: PD, pharmacology
 disoxaril: PD, pharmacology
 imipramine: PD, pharmacology
 intercellular adhesion molecule 1: EC, endogenous compound
 interferon: AE, adverse drug reaction
 interferon: DO, drug dose
 interferon: DT, drug therapy
 interferon: NA, intranasal drug administration
 interleukin 8: EC, endogenous compound
 low density lipoprotein receptor: EC, endogenous compound
 rupintrivir: AE, adverse drug reaction
 rupintrivir: DT, drug therapy
 vascular cell adhesion molecule 1: EC, endogenous compound
 virus receptor: EC, endogenous compound
 (amitriptyline) 50-48-6, 549-18-8; (disoxaril)
 87495-31-6; (imipramine) 113-52-0, 50-49-7;
 (intercellular adhesion molecule 1) 126547-89-5;
 (interleukin 8) 114308-91-7; (rupintrivir) 223537-30-2
 ag7088; win 51711

CAS REGISTRY NO.:

CHEMICAL NAME:

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ACCESSION NUMBER: 2007085532 EMBASE Full-text

TITLE: Liver cell death and anemia in Wilson disease involve acid sphingomyelinase and ceramide.

AUTHOR: Lang, Philipp A.; Nicolay, Jan P.; Kempe, Daniela S.;
 Lupescu, Adrian; Koka, Saisudha; Eisele, Kerstin; Klarl,
 Barbara A.; Huber, Stephan M.; Wieder, Thomas; Lang,
 Florian

CORPORATE SOURCE: Institute of Physiology, University of Tübingen, 72076
 Tübingen, Germany. florian.lang@uni-tuebingen.de

AUTHOR: Schenck, Marcus; Gulbins, Erich (correspondence)

10/524815

CORPORATE SOURCE: Institute of Molecular Biology, University of
Duisburg-Essen, 45122 Essen, Germany. erich.gulbins@uni-due
.de

AUTHOR: Schenck, Marcus; Rubben, Herbert

CORPORATE SOURCE: Department of Urology, University of Duisburg-Essen, 45122
Essen, Germany.

AUTHOR: Becker, Jan Ulrich; Schmid, Kurt W.

CORPORATE SOURCE: Institute of Pathology and Neuropathology, University of
Duisburg-Essen, 45122 Essen, Germany.

AUTHOR: Mann, Klaus

CORPORATE SOURCE: Department of Internal Medicine, University Clinic,
University of Duisburg-Essen, 45122 Essen, Germany.

AUTHOR: Hildenbrand, Sibylle

CORPORATE SOURCE: Department of Occupational and Social Medicine, University
of Tübingen, 72076 Tübingen, Germany.

AUTHOR: Hefter, Harald

CORPORATE SOURCE: Department of Neurology, University of Düsseldorf, 40225
Düsseldorf, Germany.

AUTHOR: Erhardt, Andreas; Haussinger, Dieter

CORPORATE SOURCE: Department of Gastroenterology, Hepatology and
Infectiology, University of Düsseldorf, 40225 Düsseldorf,
Germany.

AUTHOR: Wieder, Thomas

CORPORATE SOURCE: Department of Dermatology, University of Tübingen, 72076
Tübingen, Germany.

SOURCE: Nature Medicine, (Feb 2007) Vol. 13, No. 2, pp. 164-170.
Refs: 45
ISSN: 1078-8956; E-ISSN: 1546-170X CODEN: NAMEFI

PUBLISHER IDENT.: NM1539

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Mar 2007
Last Updated on STN: 14 Mar 2007

ABSTRACT: Wilson disease is caused by accumulation of Cu²⁺ in cells, which
results in liver cirrhosis and, occasionally, anemia. Here, we show that Cu²⁺
triggers hepatocyte apoptosis through activation of acid sphingomyelinase (Asm)
and release of ceramide. Genetic deficiency or pharmacological inhibition of
Asm prevented Cu²⁺-induced hepatocyte apoptosis and protected rats, genetically
prone to develop Wilson disease, from acute hepatocyte death, liver failure and
early death. Cu²⁺ induced the secretion of activated Asm from leukocytes,
leading to ceramide release in and phosphatidylserine exposure on erythrocytes,
events also prevented by inhibition of Asm. Phosphatidylserine exposure
resulted in immediate clearance of affected erythrocytes from the blood in
mice. Accordingly, individuals with Wilson disease showed elevated plasma
levels of Asm, and displayed a constitutive increase of ceramide- and
phosphatidylserine-positive erythrocytes. Our data suggest a previously
unidentified mechanism for liver cirrhosis and anemia in Wilson disease.
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CONTROLLED TERM: Medical Descriptors:
adult
*anemia
animal cell
apoptosis

article
 blood level
 *cell death
 controlled study
 drug activation
 drug inhibition
 erythrocyte
 female
 human
 leukocyte
 liver cell
 liver cirrhosis
 liver failure
 mouse
 nonhuman
 priority journal
 protein deficiency: DT, drug therapy
 *Wilson disease: DT, drug therapy
 Drug Descriptors:
 amitriptyline: DT, drug therapy
 amitriptyline: IP, intraperitoneal drug administration
 *ceramide
 copper
 penicillamine: DT, drug therapy
 phosphatidylserine
 *sphingomyelin phosphodiesterase: PD, pharmacology
 trientine: DT, drug therapy
 (amitriptyline) 50-48-6, 549-18-8; (copper)
 15158-11-9, 7440-50-8; (penicillamine) 2219-30-9, 52-67-5;
 (sphingomyelin phosphodiesterase) 9031-54-3; (trientine)
 112-24-3, 38260-01-4

CONTROLLED TERM:

CAS REGISTRY NO.:

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ACCESSION NUMBER: 2000418614 EMBASE Full-text
 TITLE: Physiology of apoptosis.
 AUTHOR: Gulbins, E. (correspondence); Jekle, A.; Ferlinz, K.; Grassme, H.; Lang, F.
 CORPORATE SOURCE: Dept. of Physiology, Univ. of Tuebingen, Gmelinstrasse 5, 72076 Tuebingen, Germany. erich.gulbins@uni-tuebingen.de
 SOURCE: American Journal of Physiology - Renal Physiology, (2000) Vol. 279, No. 4 48-4, pp. F605-F615.
 Refs: 113
 ISSN: 0363-6127 CODEN: AJPPFK
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 14 Dec 2000
 Last Updated on STN: 14 Dec 2000

ABSTRACT: Ion fluxes and volume changes of the whole cell as well as of organelles belong to the hallmarks of apoptosis; however, the molecular mechanism regulating these changes is only poorly characterized. Several ion channels in the plasma membrane, in particular the N-type K⁺ channel, the chloride channel cystic fibrosis conductance regulator, and an outward rectifying chloride channel, as well as the mitochondrial permeability transition pore, have been implicated to be involved in signal transduction cascades regulating apoptosis. Furthermore, Bcl-2-like proteins have been suggested to function, at least in part, as ion channels, because they display

some homology to bacterial pore-forming toxins. In contrast to the demonstration of the involvement of these different ion channels in apoptosis, the molecular consequences regulated by these ion channels, and finally triggering apoptosis, are almost completely unknown.

CONTROLLED TERM: Medical Descriptors:
 *apoptosis
 molecular biology
 priority journal
 review
 signal transduction

CONTROLLED TERM: Drug Descriptors:
 ceramide: EC, endogenous compound
 potassium channel
 protein bcl 2: EC, endogenous compound
 sodium channel
 sphingomyelin: EC, endogenous compound
 transmembrane conductance regulator: EC, endogenous compound

CAS REGISTRY NO.: (protein bcl 2) 219306-68-0; (sphingomyelin) 85187-10-6

L89 ANSWER 33 OF 37 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2009:215509 BIOSIS [Full-text](#)

DOCUMENT NUMBER: PREV200900215509

TITLE: Ceramide-Enriched Membrane Domains in Infectious Biology and Development.

AUTHOR(S): Becker, Katrin Anne [Reprint Author]; Gellhaus, Alexandra; Winterhager, Elke; Gulbins, Erich

CORPORATE SOURCE: Univ Duisburg Essen, Dept Mol Biol, Hufelandstr 55, D-45122 Essen, Germany

SOURCE: Quinn, PJ [Editor]; Wang, X [Editor]. Subcellular Biochemistry, (2008) pp. 523-538. Subcellular Biochemistry. Publisher: SPRINGER, 233 SPRING STREET, NEW YORK, NY 10013, UNITED STATES. Series: SUBCELLULAR BIOCHEMISTRY. ISSN: 0306-0225. ISBN: 978-1-4020-8830-8(H).

DOCUMENT TYPE: Book; (Book Chapter)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Mar 2009
 Last Updated on STN: 25 Mar 2009

ABSTRACT: Ceramide has been shown to be critically involved in multiple biological processes, for instance induction of apoptosis after ligation of death receptors or application of gamma-irradiation or UV-A light, respectively, regulation of cell differentiation, control of tumor cell growth, infection of mammalian cells with pathogenic bacteria and viruses or the control of embryo and organ development to name a few examples. Ceramide molecules form distinct large domains in the cell membrane, which may serve to re-organize cellular receptors and signalling molecules. Thus, in many conditions, ceramide may be involved in the spatial and temporal organisation of specific signalling pathways explaining the pleiotropic effects of this lipid. Here, we focus on the role of ceramide and ceramide-enriched membrane domains, respectively, in bacterial infections, in particular of the lung, and sepsis. We describe the role of ceramide for infections with *Neisseriae gonorrhoeae*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Finally, we discuss newly emerging aspects of the cellular function of ceramide, i.e. its role in germ line and embryo development.

CONCEPT CODE: Genetics - Animal 03506
 Biochemistry studies - General 10060
 Biochemistry studies - Lipids 10066
 Digestive system - Pathology 14006

Respiratory system - Physiology and biochemistry 16004
 Respiratory system - Pathology 16006
 Development and Embryology - Pathology 25503
 Physiology and biochemistry of bacteria 31000
 Virology - General and methods 33502
 Medical and clinical microbiology - General and methods 36001
 Medical and clinical microbiology - Bacteriology 36002
 Major Concepts
 Biochemistry and Molecular Biophysics; Infection
 INDEX TERMS: Parts, Structures, & Systems of Organisms
 lung; respiratory system; cell membrane
 INDEX TERMS: Diseases
 bacterial infection: bacterial disease
 Bacterial Infections (MeSH)
 INDEX TERMS: Diseases
 sepsis: infectious disease
 Sepsis (MeSH)
 INDEX TERMS: Diseases
 cystic fibrosis: respiratory system disease, genetic
 disease, congenital disease, digestive system disease
 Cystic Fibrosis (MeSH)
 INDEX TERMS: Chemicals & Biochemicals
 ceramide; death receptors; ceramide-enriched membrane
 domains
 INDEX TERMS: Methods & Equipment
 gamma-irradiation: therapeutic and prophylactic
 techniques, clinical techniques; UV-A light: laboratory
 techniques, spectrum analysis techniques
 INDEX TERMS: Miscellaneous Descriptors
 apoptosis; cell differentiation; cell growth; organ
 development; embryo development
 ORGANISM: Classifier
 Mammalia 85700
 Super Taxa
 Vertebrata; Chordata; Animalia
 Organism Name
 mammal (common)
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates,
 Nonhuman Mammals, Vertebrates
 ORGANISM: Classifier
 Micrococcaceae 07702
 Super Taxa
 Gram-Positive Cocci; Eubacteria; Bacteria;
 Microorganisms
 Organism Name
 Staphylococcus aureus (species): pathogen
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms
 ORGANISM: Classifier
 Neisseriaceae 06507
 Super Taxa
 Gram-Negative Aerobic Rods and Cocci; Eubacteria;
 Bacteria; Microorganisms
 Organism Name
 Neisseria gonorrhoeae (species): pathogen
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms
 ORGANISM: Classifier

Viruses 03000
 Super Taxa
 Microorganisms
 Organism Name
 Virus (common): pathogen
 Taxa Notes
 Microorganisms, Viruses

REGISTRY NUMBER: 104404-17-3 (ceramide)

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ACCESSION NUMBER: 2004:111812 BIOSIS Full-text

DOCUMENT NUMBER: PREV200400114499

TITLE: Role and biophysics of ceramide in bacterial and viral infections.

AUTHOR(S): Gulbins, Erich [Reprint Author]

CORPORATE SOURCE: Dept. of Molecular Biology, University of Duisburg-Essen, Essen, Germany

SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 194a. print.

Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004.

Biophysical Society.

ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Feb 2004

Last Updated on STN: 25 Feb 2004

ABSTRACT: We have recently shown that infection of mammalian lung epithelial cells with *P. aeruginosa* results in an activation of the acid sphingomyelinase (ASM) and a translocation of the enzyme onto the extracellular leaflet of the cell membrane. The activity of the ASM triggers the release of ceramide that reorganizes small membrane rafts to larger platforms. Ceramide enriched membrane platforms serve to cluster receptor molecules, e.g. CFTR and CD95, that mediate infection with *P. aeruginosa*. Here, we show that a very similar concept applies to infection of epithelial cells with human rhinovirus and *Salmonella typhimurium*. Rhinovirus induces an activation of the ASM and the formation of very large ceramide-enriched membrane platforms that co-localize with colera-toxin suggesting that they are formed by the fusion of small membrane rafts. These ceramide-enriched membrane platforms are required for the infection with rhinovirus since destruction of membrane rafts or inhibition of the ASM prevents viral uptake and, thus, infection. Likewise, *S. typhimurium* is internalized via ceramide-enriched membrane platforms that are formed by activation of the ASM. In addition, the fusion of the intracellular phagosome containing *S. typhimurium* with phagosomes to form a phagolysosome also requires activity of the acid sphingomyelinase and release of ceramide in the vesicle membrane. Similar data were obtained with BCG mycobacteria. The fusion of intracellular phagosomes that contain the bacteria with lysosomes requires ASM activity and formation of ceramide, while the uptake of BCG seems to be independent of ASM. Thus, ceramide-enriched membrane domains serve as "entrance gates" for several pathogens and, in addition, are critically involved in the fusion of phagosomes with lysosomes.

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520

Cytology - General 02502

Biochemistry studies - General 10060

Biochemistry studies - Lipids 10066

Enzymes - General and comparative studies: coenzymes 10802

Morphology and cytology of bacteria 30500
 Physiology and biochemistry of bacteria 31000
 Virology - General and methods 33502
 Medical and clinical microbiology - Virology 36006
 INDEX TERMS: Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology;
 Infection
 INDEX TERMS: Parts, Structures, & Systems of Organisms
 intracellular phagosomes, fusion; lysosomes; phagosome
 INDEX TERMS: Diseases
 bacterial infection: bacterial disease
 Bacterial Infections (MeSH)
 INDEX TERMS: Diseases
 viral infection: viral disease
 Virus Diseases (MeSH)
 INDEX TERMS: Chemicals & Biochemicals
 acid sphingomyelinase [EC 3.1.4.12]: activation;
 ceramide: formation
 ORGANISM: Classifier
 Enterobacteriaceae 06702
 Super Taxa
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria;
 Bacteria; Microorganisms
 Organism Name
 Salmonella typhimurium (species)
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms
 ORGANISM: Classifier
 Picornaviridae 03603
 Super Taxa
 Positive Sense ssRNA Viruses; Viruses; Microorganisms
 Organism Name
 Rhinovirus (genus): pathogen
 Taxa Notes
 Microorganisms, Positive Sense Single-Stranded RNA
 Viruses, Viruses
 ORGANISM: Classifier
 Pseudomonadaceae 06508
 Super Taxa
 Gram-Negative Aerobic Rods and Cocci; Eubacteria;
 Bacteria; Microorganisms
 Organism Name
 Pseudomonas aeruginosa (species): pathogen
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms
 REGISTRY NUMBER: 9031-54-3 (acid sphingomyelinase)
 9031-54-3 (EC 3.1.4.12)
 104404-17-3 (ceramide)

L89 ANSWER 35 OF 37 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
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 ACCESSION NUMBER: 2002:362613 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200200362613
 TITLE: P. aeruginosa infects mammalian cells via membrane rafts.
 AUTHOR(S): Gulbins, E. [Reprint author]; Grassme, H. [Reprint author]
 CORPORATE SOURCE: Dept. of Molecular Biology, University of Essen,
 Hufelandstrasse 55, 45122, Essen, Germany
 SOURCE: Pfluegers Archiv European Journal of Physiology, (March,
 2002) Vol. 443, No. Supplement 1, pp. S161-S162. print.
 Meeting Info.: 81st Annual Joint Meeting of the

Physiological Society, the Scandinavian Physiological Society and the German Physiological Society. Tuebingen, Germany. March 15-19, 2002.
 CODEN: PFLABK. ISSN: 0031-6768.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 3 Jul 2002
 Last Updated on STN: 3 Jul 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
 Cytology - Animal 02506
 Biochemistry studies - Proteins, peptides and amino acids 10064
 Biophysics - Membrane phenomena 10508
 Pathology - General 12502
 Morphology and cytology of bacteria 30500
 Physiology and biochemistry of bacteria 31000
 Medical and clinical microbiology - Bacteriology 36002
 Invertebrata: comparative, experimental morphology, physiology and pathology - Aschelminthes 64016

INDEX TERMS: Major Concepts
 Infection; Membranes (Cell Biology)

INDEX TERMS: Parts, Structures, & Systems of Organisms
 cell surface; membrane raft

INDEX TERMS: Diseases
 P. aeruginosa infection: bacterial disease, pathology,
 Pseudomonas aeruginosa infection
 Pseudomonas Infections (MeSH)

INDEX TERMS: Diseases
 S. typhimurium infection: bacterial disease, pathology,
 Salmonella typhimurium infection
 Salmonella Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals
 CD95; CD95 ligand; CD95 receptor; cystic fibrosis
 conductance regulator

INDEX TERMS: Miscellaneous Descriptors
 functional type III secretion system: modulation;
 Meeting Abstract

ORGANISM: Classifier
 Enterobacteriaceae 06702
 Super Taxa
 Facultatively Anaerobic Gram-Negative Rods; Eubacteria;
 Bacteria; Microorganisms
 Organism Name
 S. typhimurium [Salmonella typhimurium]: pathogen
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms

ORGANISM: Classifier
 Mammalia 85700
 Super Taxa
 Vertebrata; Chordata; Animalia
 Organism Name
 mammal
 Taxa Notes
 Animals, Chordates, Mammals, Nonhuman Vertebrates,
 Nonhuman Mammals, Vertebrates

ORGANISM: Classifier
 Nematoda 51300
 Super Taxa

Aschelminthes; Helminthes; Invertebrata; Animalia
 Organism Name
 Caenorhabditis elegans [worm]: host
 Taxa Notes
 Animals, Aschelminthes, Helminths, Invertebrates
 ORGANISM: Classifier
 Pseudomonadaceae 06508
 Super Taxa
 Gram-Negative Aerobic Rods and Cocci; Eubacteria;
 Bacteria; Microorganisms
 Organism Name
 P. aeruginosa [Pseudomonas aeruginosa]: pathogen
 Taxa Notes
 Bacteria, Eubacteria, Microorganisms
 REGISTRY NUMBER: 81271-93-4 (CD95)
 GENE NAME: Caenorhabditis elegans ced 3 gene (Nematoda): activation,
 regulation; Caenorhabditis elegans ced 4 gene (Nematoda):
 activation, regulation

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ACCESSION NUMBER: 2002:596410 BIOSIS Full-text
 DOCUMENT NUMBER: PREV200200596410
 TITLE: Molecular mechanisms of pulmonary P. aeruginosa infections.
 AUTHOR(S): Gulbins, E. [Reprint author]; Grassme, H. [Reprint author]
 CORPORATE SOURCE: Dept. of Molecular Biology, University of Essen,
 Hufelandstrasse 55, 45122, Essen, Germany
 SOURCE: International Journal of Molecular Medicine, (2002) Vol.
 10, No. Supplement 1, pp. S95. print.
 Meeting Info.: 7th World Congress on Advances in Oncology
 and the 5th International Symposium on Molecular Medicine.
 Hersonissos, Crete, Greece. October 10-12, 2002.
 ISSN: 1107-3756.

DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 20 Nov 2002
 Last Updated on STN: 20 Nov 2002
 CONCEPT CODE: General biology - Symposia, transactions and proceedings
 00520
 Cytology - Animal 02506
 Cytology - Human 02508
 Genetics - Human 03508
 Biochemistry studies - Proteins, peptides and amino acids
 10064
 Biochemistry studies - Lipids 10066
 Enzymes - General and comparative studies: coenzymes
 10802
 Metabolism - Metabolic disorders 13020
 Digestive system - Pathology 14006
 Respiratory system - Physiology and biochemistry 16004
 Respiratory system - Pathology 16006
 Physiology and biochemistry of bacteria 31000
 Medical and clinical microbiology - Bacteriology 36002
 INDEX TERMS: Major Concepts
 Infection; Respiratory System (Respiration)
 INDEX TERMS: Parts, Structures, & Systems of Organisms
 lung epithelial cells: respiratory system, apoptosis
 INDEX TERMS: Diseases
 cystic fibrosis: digestive system disease, genetic

disease, metabolic disease, respiratory system disease
Cystic Fibrosis (MeSH)

INDEX TERMS: Diseases
pulmonary *Pseudomonas aeruginosa* infection: bacterial
disease, respiratory system disease, etiology
Pseudomonas Infections (MeSH)

INDEX TERMS: Chemicals & Biochemicals
CD95; CD95 ligand; acid sphingomyelinase; ceramide

INDEX TERMS: Miscellaneous Descriptors
molecular mechanisms; Meeting Abstract

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates,
Vertebrates

ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria;
Bacteria; Microorganisms
Organism Name
P. aeruginosa [*Pseudomonas aeruginosa*]: pathogen
Taxa Notes
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 81271-93-4 (CD95)
9031-54-3 (acid sphingomyelinase)
104404-17-3 (ceramide)

L89 ANSWER 37 OF 37 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN

ACCESSION NUMBER: 2001:248593 BIOSIS Full-text

DOCUMENT NUMBER: PREV200100248593

TITLE: Involvement of mitochondria and stress activated kinases in
P. aeruginosa induced apoptosis.

AUTHOR(S): Jendrossek, V. [Reprint author]; Grassme, H.; Mueller, I.;
Lang, F.; Gulbins, E.

CORPORATE SOURCE: Dept. of Physiology, University of Tuebingen, Gmelinstrasse
5, 72076, Tuebingen, Germany

SOURCE: Pfluegers Archiv European Journal of Physiology, (2001)
Vol. 441, No. 6 Supplement, pp. R141. print.
Meeting Info.: Joint Congress of the Scandinavian and the
German Physiological Societies. Berlin, Germany. March
10-13, 2001.
CODEN: PFLABK. ISSN: 0031-6768.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002

CONCEPT CODE: Medical and clinical microbiology - Bacteriology 36002
General biology - Symposia, transactions and proceedings
00520
Cytology - General 02502
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes
10802

10/524815

Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Cell
Biology; Infection
INDEX TERMS: Parts, Structures, & Systems of Organisms
mitochondria
INDEX TERMS: Diseases
Pseudomonas aeruginosa infection: bacterial disease
Pseudomonas Infections (MeSH)
INDEX TERMS: Chemicals & Biochemicals
Jun N-terminal kinases: activation; cystic fibrosis
conductance regulator; cytochrome c: release; reactive
oxygen intermediates: synthesis; stress activated
kinases
INDEX TERMS: Miscellaneous Descriptors
apoptosis; cellular depolarization; cellular signaling;
immunocompromization; Meeting Abstract
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Chang cell line: human conjunctiva epithelial cells
human: patient
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates,
Vertebrates
ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria;
Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa: pathogen, strain-PAO-I
Taxa Notes
Bacteria, Eubacteria, Microorganisms
REGISTRY NUMBER: 9007-43-6 (cytochrome c)

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCaplus now includes complete International Patent Classification (IPC)
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ANTI DEPRESSANT?/BI

L24 15309 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON ?CYSTIC FIBROS?/BI

L25 609 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR
FIBRO CYSTIC?/BI

L26 155 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI

L27 5892 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON CFTR/BI

L28 15430 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROSIS/BI (L)
CYSTIC/BI

L29 16341 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR
L27 OR L28)

L32 9 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON L23 AND (TRICYCLIC?/BI
OR TETRACYCLIC?/BI) AND L29

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E OR TRIMIPRAMINE)/CN

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L14 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR
DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR
METAPRAMINE)/CN

L15 4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR
NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN

L16 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR
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FLUOTRACEN)/CN

L17 25 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14
OR L15 OR L16)

L19 6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMOXAPINE OR
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FIBRO CYSTIC?/BI

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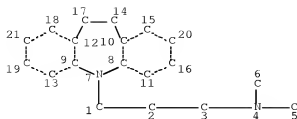
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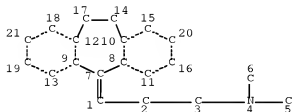
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 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE
 L5 STR



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

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L9	83	SEA FILE=REGISTRY FAM FUL L5				
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L25	609	SEA FILE=ZCAPLUS SPE=ON	ABB=ON	PLU=ON	FIBROCYSTIC?/BI	
		FIBRO CYSTIC?/BI				
L26	155	SEA FILE=ZCAPLUS SPE=ON	ABB=ON	PLU=ON	MUCOVISCIDOSIS/BI	
L27	5892	SEA FILE=ZCAPLUS SPE=ON	ABB=ON	PLU=ON	CFTR/BI	
L28	15430	SEA FILE=ZCAPLUS SPE=ON	ABB=ON	PLU=ON	FIBROSIS/BI (L)	
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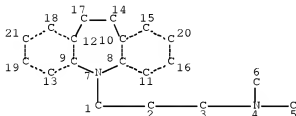
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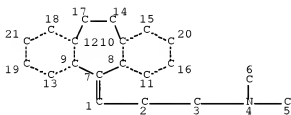
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DEFAULT ECLEVEL IS LIMITED
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NUMBER OF NODES IS 21
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STEREO ATTRIBUTES: NONE
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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
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L9          83 SEA FILE=REGISTRY FAM FUL L5
L12         6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR
              CLOMIPRAMINE OR DOSULEPIN OR DOTHIEPIN OR DOXEPIN OR LOFEPRAMIN
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NORTRIPTYLINE OR PROTRIPTYLINE)/CN
L14      6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR
DIBENZEPIN OR DIMETACRINE OR IPRINDOLE OR MELITRACEN OR
METAPRAMINE)/CN
L15      4 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR
NOXIPTILINE OR PROPIZEPINE OR QUINUPRAMINE)/CN
L16      6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMINEPTINE OR
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OR L15 OR L16)
L19      6 SEA FILE=REGISTRY SPE=ON ABB=ON PLU=ON (AMOXAPINE OR
MAPROTILINE OR MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR
OXAPROTILINE)/CN
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CYSTIC/BI
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L27 OR L28)
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L48      96337 SEA L29
L49      39 SEA L47 AND L48
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L54      25 SEA L53 AND L29
L56      24 SEA (TRICYCLIC OR TETRACYCLIC)/BI AND L29
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L58      31 SEA L57 AND PY<2004

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 PROCESSING COMPLETED FOR L58

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L91      49 DUP REM L90 L58 (4 DUPLICATES REMOVED)
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ANSWERS '23-27' FROM FILE MEDLINE
ANSWERS '28-48' FROM FILE EMBASE
ANSWER '49' FROM FILE BIOSIS

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10/524815

=> d ibib abs hitind hitstr L91 1-22; d iall L91 23-49

L91 ANSWER 1 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2009:1044258 ZCAPLUS Full-text
 DOCUMENT NUMBER: 151:297806
 TITLE: Methods and compositions for the treatment of disorders associated with defects of the cystic fibrosis transmembrane conductance regulator gene or protein
 INVENTOR(S): Lin, Stephen; Staunton, Jane; Sui, Jinliang
 PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA
 SOURCE: PCT Int. Appl., 108pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2009105234	A2	20090827	WO 2009-US1061	20090219
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.: US 2008-66259P P 20080219				
AB	The present invention features compns., methods, and kits for treating, or ameliorating disorders associated with a defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or protein (e.g., cystic fibrosis).			
CC	63-5 (Pharmaceuticals)			
ST	Section cross-reference(s): 6			
ST	defect cystic fibrosis transmembrane conductance regulator gene protein CFTR			
IT	Gene, animal			
IT	RL: BSU (Biological study, unclassified); BIOL (Biological study) (CFTR; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)			
IT	Essential oils			
IT	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Clary sage; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)			
IT	Essential oils			
IT	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cedarwood; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)			
IT	Essential oils			
IT	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (clove; methods and compns. for treatment of disorders associated with			

- defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT Cystic fibrosis
 - Drug design
 - Drug screening
 - Drug targets
 - HMG-CoA reductase inhibitors
 - Human
 - Inhalation drug delivery systems
 - Leiurus quinquestriatus
 - Oral drug delivery systems
 - (methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT CFTR (cystic fibrosis transmembrane conductance regulator)
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT Flavonoids
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT Steroids
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 853220-7
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (APWAG1; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 95907-66-7D, Quinoxalinecarboxylic acid, derivs.
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (BML-257; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 2390-54-7D, derivs.
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (BTA-1; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 77-10-1D, derivs., hydrochlorides
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (BTCP; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 331-39-5D, Caffeic acid, derivative
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (CAPE; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 119-65-3D, Isoquinoline, derivative
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (CBIQ; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)

- IT 51-17-2D, Benzimidazole, derivative
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DCEB10; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 289-95-2D, Pyrimidine, derivative
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PP2; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 9076-57-7, Histone deacetylase 26833-87-4, Homoharringtonine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor III; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 155215-87-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 131384-38-8, Farnesyltransferase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 9028-35-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)
- IT 50-22-6, Corticosterone 50-27-1, Estril 50-28-2, Estradiol, biological studies 50-48-6, Amitriptyline 50-76-0, Dactinomycin 53-19-0, Mitotane 53-34-9, Fluprednisolone 54-11-5, Nicotine 56-53-1, Diethylstilbestrol 57-63-6, Ethinyl estradiol 57-91-0, Alfatradiol 58-33-3, Promethazine hydrochloride 58-46-8, Tetrabenazine 58-89-9, Lindane 59-96-1 60-82-2, Phloretin 66-97-7, Psoralen 68-88-2, Hydroxyzine 70-30-4, Hexachlorophene 71-62-5, Veratridine 72-69-5, Nortriptyline 72-80-0, Chlorquinaldol 75-05-8, Acetonitrile, biological studies 79-78-7, Allyl α -ionone 83-79-4, Rotenone 84-17-3, Dienestrol 89-68-9, Chlorothymol 92-84-2, Phenothiazine 94-18-8, Benzylparaben 94-41-7, Chalcone 94-78-0, Phenazopyridine 97-18-7, Bithionol 97-23-4, Dichlorophen 97-24-5, Fenticlor 99-66-1, Valproic acid 103-16-2, Monobenzene 111-87-5, 1-Octanol, biological studies 113-59-7, Chlorprothixene 117-39-5, Quercetin 120-32-1, Clorofene 123-03-5, Cetylpyridinium chloride 124-94-7, Triamcinolone 125-69-9, Dextromethorphan hydrobromide 127-31-1, Fludrocortisone 129-03-3 130-61-0, Thioridazine hydrochloride 131-53-3 136-47-0, Tetracaine hydrochloride 140-95-4 148-82-3, Melphalan 152-43-2, Quinestrol 298-57-7, Cinnarizine 303-49-1, Clomipramine 313-04-2, Desmosterol 356-12-7, Fluocinonide 362-07-2 378-44-9, Betamethasone 402-71-1, TPCK 434-22-0, Nandrolone 439-14-5, Diazepam 440-17-5, Trifluoperazine hydrochloride 446-72-0, Genistein 483-18-1, Emetine 520-36-5, Apigenin 524-95-8 528-48-3, Fisetin 541-19-5, Suxamethonium iodide 553-08-2, Thonzonium bromide 579-23-7 583-03-9, Fenipentol 638-94-8, Desonide 719-59-5 777-11-7, Haloprogin 863-61-6, Menatetrenone 961-29-5, Isoliquiritigenin 982-57-0, Chloramphenicol sodium succinate 985-13-7, Ethavrine hydrochloride 1034-01-1, Octyl gallate 1098-60-8, Triflupromazine hydrochloride 1404-04-2, Neomycin 1420-55-9 1668-19-5, Doxepin 1716-12-7, Sodium Phenylbutyrate 1744-22-5,

Riluzole 1841-19-6, Fluspirilene 1951-25-3, Amiodarone 2062-78-4,
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 4547-24-4, Corosolic acid 5466-77-3, Octyl methoxycinnamate 5610-40-2,
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 57808-66-9, Domperidone 58749-22-7, Licochalcone-A 59937-28-9,
 Malotilate 60142-96-3, Gabapentin 60282-87-3, Gestodene 61413-54-5,
 Rolipram 62571-86-2, Captopril 62996-74-1, Staurosporine 63653-99-6,
 FS 2 63675-72-9, Nisoldipine 64706-54-3, Bepridil 64872-76-0,
 Butoconazole 65472-88-0, Naftifine 65899-73-2 66085-59-4, Nimodipine
 66575-29-9, Forskolin 66934-18-7 68506-86-5 68786-66-3,
 Triclabendazole 70238-51-6 70288-86-7, Ivermectin 71145-03-4,
 BAYK8644 71897-07-9, Tyrphostin Ag 1295 72509-76-3, Felodipine
 74863-84-6, Argatroban 75330-75-5, Lovastatin 75593-17-8,
 Debramo-hymenialdisine 75607-67-9, Fludarabine phosphate 75695-93-1,
 Isradipine 75747-14-7, 17-AAG 78491-02-8, Diazolidinyl urea
 79794-75-5, Loratadine 79855-88-2, Trequinsin 79902-63-9, Simvastatin
 81117-35-3, N-Nonyldeoxynojirimycin 81166-47-4, DIOA 81226-60-0
 82749-70-0, DCPIB 90357-06-5, Bicalutamide 91599-74-5, Benidipine
 hydrochloride 93957-54-1, Fluvastatin 95734-82-0, Nedaplatin
 98629-43-7, Gusperimus 100427-26-7, Lercanidipine 101477-55-8,
 Lomerizine 101975-10-4, Zardaverine 102146-07-6,
 8-Cyclopentyl-1,3-dipropylxanthine 102396-24-7, Jasplakinolide
 103060-53-3, Daptomycin 103177-37-3, Pramlukast 103577-45-3,
 Lansoprazole 103745-39-7, HA 1077 104615-18-1, CGS15943 104632-26-0,
 Pramipexole 104757-53-1, Barnidipine hydrochloride 106266-06-2,
 Risperidone 106328-57-8, BW-A4C 107254-86-4,

5-Nitro-2-(3-phenyl-propylamino) benzoic acid

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)

- IT 107753-78-6, Zafirlukast 110429-36-2, N-Methyl-paroxetine 110588-57-3, Saperconazole 111470-99-6, Amlodipine besylate 112809-51-5, Letrozole 112830-95-2, HU 210 113665-84-2, Clopidogrel 116666-63-8, Mibefradil dihydrochloride 117976-89-3, Rabeprazole 118457-14-0, Nebivolol 120014-06-4, Donepezil 120934-96-5, FPL64176 121911-71-5 122320-73-4 123318-82-1, Clofarabine 123524-52-7, Azelnidipine 123653-11-2, NS 398 124753-97-5, C6-Ceramide 126544-47-6, Ciclesonide 130493-03-7, Bimocinolol 130495-35-1, SKF-96365 131543-22-1, WIN 55212-2 132203-70-4, Cilnidipine 132861-87-1, PD81723 133343-34-7, Lactacystin 133407-82-6, MG 132 133550-35-3, AG 494 134381-21-8, Epoxomicin 134523-00-5, Atorvastatin 138605-00-2, NKH477 138989-57-8, RG 14620 139755-83-2, Sildenafil 141797-92-4 145599-86-6, Cerivastatin 145915-58-8 145915-60-2 147098-20-2, Rosuvastatin calcium 148016-81-3, Doripenem 148741-30-4, AG 879 149647-78-9, Suberoylanilide hydroxamic acid 154447-36-6, LY294002 154598-52-4, Efavirenz 159351-69-6, Everolimus 160098-96-4, SCH58261 161814-49-9, Amprenavir 162401-32-3, Roflumilast 163222-33-1, Ezetimibe 163515-35-3, Chlorotoxin 167869-21-8, PD98059 168835-82-3, SU1498 169590-42-5, Celecoxib 179324-69-7, Bortezomib 180977-44-0, GGTI-298 183506-66-3 186131-38-4, WP631 189197-69-1, Ro 48-8071 191102-87-1, GGTI-2147 191114-48-4, Telithromycin 192441-08-0, Lomeguatrib 193551-00-7, CAY10398 193620-69-8, TAS-301 203460-30-4, SNX-482 209783-80-2 212141-54-3, Vatalanib 212844-53-6, Purvalanol A 218924-25-5, KNK-437 221877-54-9, Zotarolimus 223499-30-7, YM 58483 224785-90-4 225235-77-8 239066-73-0, AL 438 269390-69-4 287383-59-9, Scriptaid 287714-41-4, Rosuvastatin 289893-25-0, Arimocinolol 293754-55-9, TO 901317 298193-32-5 302962-49-8, Dasatinib 324526-70-7 357400-13-6, NNC55-0396 362000-44-0 371935-74-9, PI-103 421580-53-2 433695-36-4, BRL-50481 439083-90-6, BAY60-7550 467214-20-6 496864-16-5, Aloisina A 537034-15-4 544478-19-5, MRS1845 546141-08-6, URB597 623531-00-0 698387-09-6, Neratinib 749886-87-1 815592-21-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)

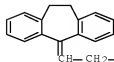
- IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline 303-49-1, Clomipramine 1668-19-5, Doxepin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for treatment of disorders associated with defects of cystic fibrosis transmembrane conductance regulator gene or protein)

- RN 50-48-6 ZCAPLUS

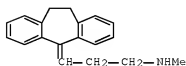
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)

CH₂-CH₂-CH₂-NMe₂

10/524815

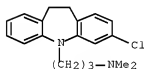
RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



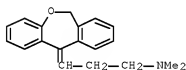
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



L91 ANSWER 2 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:827242 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 151:108500

TITLE: Pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants

INVENTOR(S): Gulbins, Erich

PATENT ASSIGNEE(S): Cycnad GmbH & Co. KG, Germany

SOURCE: PCT Int. Appl., 54pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
	W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
	PRIORITY APPLN. INFO.:			DE 2007-102007063535A	20071221
AB	The invention relates to a pharmaceutical compound for the prophylaxis and/or symptomatic treatment of cystic fibrosis, particularly for the prophylaxis and/or treatment of infections and/or infection illnesses manifesting with cystic fibrosis, having at least one anti-depressive and preferable at least one dispersion agent and/or at least one pharmaceutically tolerated carrier material. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus Cftr-knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration				
IC	ICM A61K				
CC	63-6 (Pharmaceuticals)				
ST	Section cross-reference(s): 1, 14				
IT	cystic fibrosis antidepressant inhalant 5-HT reuptake inhibitors Antidepressants Burkholderia cepacia Cystic fibrosis Dopamine reuptake inhibitors Haemophilus influenzae Inhalation drug delivery systems Lung Noradrenaline reuptake inhibitors Parenteral drug delivery systems Pharmaceutical solutions Prophylaxis Pseudomonas aeruginosa Staphylococcus aureus Therapy (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)				
IT	Antibodies and Immunoglobulins RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)				
IT	111-57-9, Ceramid 9031-54-3, Sphingomyelinase RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)				
IT	50-67-9, Serotonin, biological studies 51-41-2, Noradrenalin 51-61-6, Dopamine, biological studies RL: BSU (Biological study, unclassified); BIOL (Biological study)				

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline
 50-49-7, Imipramine 58-40-2, Promazine 72-69-5,
 Nortriptyline 86-13-5, Benzotropine 113-45-1, Methylphenidate
 129-03-3, Cyproheptadine 155-09-9, Tranylcypromine 256-96-2D,
 5H-Dibenz[b,f]azepine, derivative 303-49-1 303-53-7,
 Cyclobenzaprine 315-72-0 494-19-9,
 10,11-Dihydro-5H-dibenzo[b,f]azepine 739-71-9, Trimipramine
 911-45-5, Clomiphen 1668-19-5, Doxepine 4317-14-0,
 Amitriptyline oxide 4498-32-2, Dibenzepine 6621-47-2,
 Perhexiline 10262-69-8, Maprotiline 19794-93-5, Trazodon
 23047-25-8, Lofepramine 24219-97-4, Mianserin
 24526-64-5, Nomifensin 32359-34-5, Medifoxamine 34911-55-2, Bupropion
 46817-91-8, Viloxazine 54739-18-3, Fluvoxamine 57574-09-1,
 Amineptine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71320-77-9,
 Moclobemide 71620-89-8, Reboxetine 72797-41-2, Tianeptine
 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 92623-85-3,
 Milnacipran 93413-69-5, Venlafaxin 116539-59-4, Duloxetine
 128196-01-0, Escitalopram

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

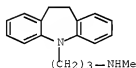
(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

IT 50-47-5, Desipramine 50-48-6, Amitriptyline
 50-49-7, Imipramine 72-69-5, Nortriptyline
 303-49-1 315-72-0 739-71-9, Trimipramine
 1668-19-5, Doxepine 4498-32-2, Dibenzepine
 10262-69-8, Maprotiline 23047-25-8, Lofepramine
 24219-97-4, Mianserin 57574-09-1, Amineptine
 72797-41-2, Tianeptine 85650-52-8, Mirtazapine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)

RN 50-47-5 ZCAPLUS

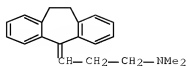
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX NAME)



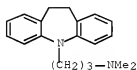
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)

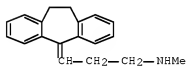
10/524815



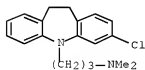
RN 50-49-7 ZCAPLUS
CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)

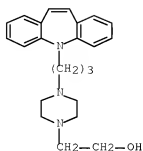


RN 303-49-1 ZCAPLUS
CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



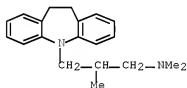
RN 315-72-0 ZCAPLUS
CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX NAME)

10/524815



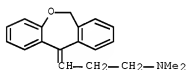
RN 739-71-9 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl- (CA INDEX NAME)



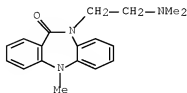
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



RN 4498-32-2 ZCAPLUS

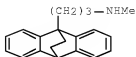
CN 11H-Dibenzo[b,e][1,4]diazepin-11-one, 10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



10/524815

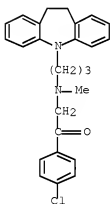
RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



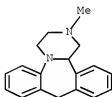
RN 23047-25-8 ZCAPLUS

CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)



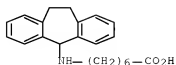
RN 24219-97-4 ZCAPLUS

CN Dibenzo[c,f]pyrazino[1,2-a]azepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



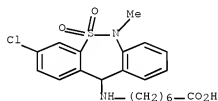
RN 57574-09-1 ZCAPLUS

CN Heptanoic acid, 7-[(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)amino]- (CA INDEX NAME)



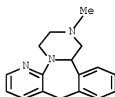
RN 72797-41-2 ZCAPLUS

CN Heptanoic acid, 7-[(3-chloro-6,11-dihydro-6-methyl-5,5-dioxidodibenzo[c,f][1,2]thiazepin-11-yl)amino]- (CA INDEX NAME)



RN 85650-52-8 ZCAPLUS

CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine, 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L91 ANSWER 3 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:206116 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 150:252701

TITLE: Therapeutic combinations useful in treating cystic fibrosis and other CFTR-related diseases

INVENTOR(S): Singh, Ashvani; Worley, Jennings Franklin., III; Zlokarnik, Gregor

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 65pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO	2009023509	A2	20090219	WO	2008-US72446	20080807
W:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW 					
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GD, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					

PRIORITY APPLN. INFO.: US 2007-954850P P 20070809

AB The invention discloses therapeutic combinations and kits useful in treating CFTR-related diseases, such as cystic fibrosis. Combinations of the invention include e.g. ivermectin and N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide.

CC 1-12 (Pharmacology)

ST CFTR disease cystic fibrosis combination treatment; quinoline carboxamide deriv combination ivermectin CFTR disease treatment

IT CFTR (cystic fibrosis transmembrane conductance regulator)
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (508-dephenylalanine-; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT Mutation
 (mutant CFTR; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT CFTR (cystic fibrosis transmembrane conductance regulator)
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (mutant; therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT Antifibrotic agents
 Combination chemotherapy
 Cystic fibrosis
 Drug delivery systems
 Human
 (therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT 16887-00-6, Chloride, biological studies
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

IT 50-41-9, Clomiphene citrate 50-52-2, Thioridazine 55-03-8, Levothyroxine sodium 58-33-3, Promethazine hydrochloride 58-39-9, Perphenazine 69-09-0, Chlorpromazine hydrochloride 83-43-2, Methylprednisolone 84-02-6, Prochlorperazine maleate 129-20-4, Oxyprenbutazone 154-42-7, Thioguanine 894-71-3, Nortriptyline hydrochloride 969-33-5, Cyproheptadine hydrochloride 1225-55-4, Protriptyline hydrochloride 1951-25-3, Amiodarone 3810-80-8, Diphenoxylate hydrochloride 4330-99-8, Trimeprazine tartrate 14028-44-5, Amoxapine 14976-57-9, Clemastine fumarate 17321-77-6, Chlorimipramine hydrochloride 19216-56-9 42971-09-5,

Vinpocetine 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54527-84-3, Nicardipine hydrochloride 55981-09-4, Nitazoxanide 59865-13-3, Cyclosporine A 64706-54-3, Bepridil 70288-86-7, Ivermectin 72956-09-3, Carvedilol 79794-75-5, Loratadine 84625-61-6, Itraconazole 85650-52-8, Mirtazapine 93957-55-2, Fluvastatin sodium 100643-71-8, Desloratadine 110429-35-1, Paroxetine hydrochloride hemihydrate 111470-99-6, Amlodipine besylate 116666-63-8, Mibefradil dihydrochloride 127779-20-8, Saquinavir 159989-65-8, Nelfinavir mesylate 163222-33-1, Ezetimibe 184475-35-2, Gefitinib 325779-54-2 329691-97-6 329691-99-8 329692-01-5
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combinations for treatment of cystic fibrosis and other CFTR-related diseases)

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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(therapeutic combinations for treatment of cystic
fibrosis and other CFTR-related diseases)

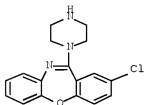
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

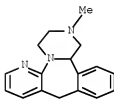
(therapeutic combinations for treatment of cystic
fibrosis and other CFTR-related diseases)

10/524815

IT 14028-44-5, Amoxapine 85650-52-8, Mirtazapine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (therapeutic combinations for treatment of cystic
 fibrosis and other CFTR-related diseases)
 RN 14028-44-5 ZCAPLUS
 CN Dibenz[b,f][1,4]oxazepine, 2-chloro-11-(1-piperazinyl)- (CA INDEX NAME)



RN 85650-52-8 ZCAPLUS
 CN Pyrazino[2,1-a]pyrido[2,3-c][2]benzazepine,
 1,2,3,4,10,14b-hexahydro-2-methyl- (CA INDEX NAME)



L91 ANSWER 4 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2009:549944 ZCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 150:489908
 TITLE: System, method, and apparatus for storing, retrieving,
 and integrating clinical, diagnostic, genomic, and
 therapeutic data
 INVENTOR(S): Davies, Richard J.; Batye, Rick
 PATENT ASSIGNEE(S): MD Dacacor, Inc., USA
 SOURCE: U.S., 55pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 7529685	B2	20090505	US 2001-983289	20011023
PRIORITY APPLN. INFO.:			US 2001-315020P	P 20010828

AB A method, system, and computer program product for storing and retrieving patient data in a database connected to a network is disclosed. The method comprises storing clin. data in the database, extracting data from the clin.

data, querying the database using a taxonomy that includes inclusive or exclusive search criterion, and receiving a result set. The method comprises creating a taxonomy that includes at least one search criterion; sending a query to the database, the query including said at least one search criteria; receiving the result set in response to the query, the result set including at least one result record; and displaying said at least one result record. The method, system, and computer program product can further include a user such as a clin. researcher, a treating physician, or a consulting physician analyzing the result set. A physician enters clin. information into the system about a patient being treated with azathioprine for arthritis developing anemia and showing neg. for GI bleeding. The system generates a result set that includes a suggestion to the physician to test the patient for a mutation in her thiopurine S-methyltransferase (TPMT) gene locus. The patient is found to be heterozygous for mutant TPMT which results in severe hematopoietic toxicity and resultant anemia. The system suggests alternative non-TPMT metabolized antiarthritic medication.

INCL 705003000; 707005000; 704009000

CC 9-1 (Biochemical Methods)

Section cross-reference(s): 1, 3, 14

IT Cystic fibrosis

(and modifier genes; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

IT 549-18-8, Elavil 56296-78-7, Prozac

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(depression treatment with, CYP2D6 variant in relation to; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

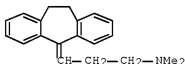
IT 549-18-8, Elavil

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(depression treatment with, CYP2D6 variant in relation to; system, method, and apparatus for storing, retrieving, and integrating clin., diagnostic, genomic, and therapeutic data)

RN 549-18-8 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 5 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2009:765170 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 151:42088

TITLE: Pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants

10/524815

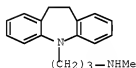
PATENT ASSIGNEE(S): Cynad G.m.b.H. & Co. K.-G., Germany
 SOURCE: Ger. Offen., 12pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 102007063535	A1	20090625	DE 2007-102007063535	20071221
WO 2009083211	A2	20090709	WO 2008-EP10996	20081222
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BG, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

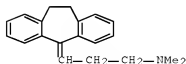
PRIORITY APPLN. INFO.: DE 2007-102007063535A 20071221

- AB The invention concerns a pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis, in particular for prophylaxis and/or treatment of cystic fibrosis related infections and/or infectious diseases, comprising at least one antidepressant and at least one dispersion medium. Liquid dispersion media are used to prepare parenteral, especially inhalant delivery systems. Thus Cfxr-knockout mice and wild-type mice were treated with 4 mg amitriptyline/L water inhalant formulations; lung exts. were tested for sphingomyelinase activity and ceramide concentration
- CC 63-6 (Pharmaceuticals)
- ST Section cross-reference(s): 1, 14
- IT cystic fibrosis antidepressant inhalant
- IT Antidepressants
- Burkholderia cepacia
- Cystic fibrosis
- Haemophilus influenzae
- Inhalation drug delivery systems
- Lung
- Parenteral drug delivery systems
- Pharmaceutical solutions
- Prophylaxis
- Pseudomonas aeruginosa
- Staphylococcus aureus
- Therapy
- (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
- IT Antibodies and Immunoglobulins
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
- IT 480-49-9, Filipin 1400-61-9, Nystatin 7585-39-9, β -Cyclodextrin
- RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (in combination with; pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with

- antidepressants)
- IT 111-57-9, Ceramid 9031-54-3, Sphingomyelinase
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
- IT 50-47-5, Desipramine 50-48-6, Amitriptyline
 50-49-7, Imipramine 72-69-5, Nortriptyline
 256-96-2D, 5H-Dibenz[b,f]azepine, derivative 303-49-1
 315-72-0 494-19-9, 10,11-Dihydro-5H-dibenzo[b,f]azepine
 739-71-9, Trimipramine 1668-19-5, Doxepine
 4317-14-0, Amitriptyline oxide 4498-32-2, Dibenzepine
 10262-69-8, Maprotiline 23047-25-8, Lofepramine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
- IT 50-47-5, Desipramine 50-48-6, Amitriptyline
 50-49-7, Imipramine 72-69-5, Nortriptyline
 303-49-1 315-72-0 739-71-9, Trimipramine
 1668-19-5, Doxepine 4498-32-2, Dibenzepine
 10262-69-8, Maprotiline 23047-25-8, Lofepramine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmaceutical composition for prophylaxis and/or symptomatic treatment of cystic fibrosis with antidepressants)
- RN 50-47-5 ZCAPLUS
- CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N-methyl- (CA INDEX NAME)

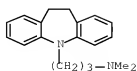


- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



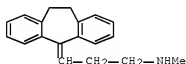
- RN 50-49-7 ZCAPLUS
- CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)

10/524815



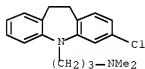
RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



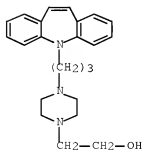
RN 303-49-1 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 315-72-0 ZCAPLUS

CN 1-Piperazineethanol, 4-[3-(5H-dibenz[b,f]azepin-5-yl)propyl]- (CA INDEX NAME)

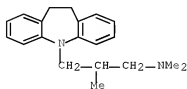


RN 739-71-9 ZCAPLUS

CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N,β-trimethyl-

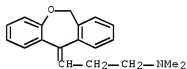
10/524815

(CA INDEX NAME)



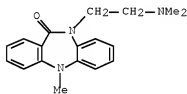
RN 1668-19-5 ZCAPLUS

CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



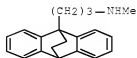
RN 4498-32-2 ZCAPLUS

CN 11H-Dibenzo[b,e][1,4]diazepin-11-one,
10-[2-(dimethylamino)ethyl]-5,10-dihydro-5-methyl- (CA INDEX NAME)



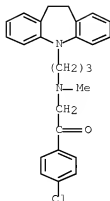
RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



RN 23047-25-8 ZCAPLUS

CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)

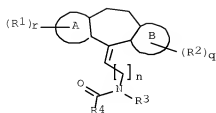


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 6 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2008:1211489 ZCAPLUS Full-text
 DOCUMENT NUMBER: 149:440406
 TITLE: Methods of using tricyclic compounds in treating sodium channel-mediated diseases or conditions
 INVENTOR(S): Kamboj, Rajender; Fraser, Robert; Fu, Jianmin; Kodumuru, Vishnumurthy; Sadalapure, Kashinath
 PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.
 SOURCE: PCI Int. Appl., 11pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008121859	A1	20081009	WO 2008-US58728	20080328
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2007-909091P P 20070330
 OTHER SOURCE(S): CASREACT 149:440406; MARPAT 149:440406
 GI



- AB This invention discloses tricyclic compds. I [$n = 1-3$; $r, q = 0-4$; A, B = fused (hetero)aryl; R1, R2 = alkyl, alkenyl, halo, etc.; R3 = H, alkyl, alkenyl, etc.; R4 = H, alkyl, halo, etc.], as a stereoisomer, enantiomer, tautomer thereof or mixts. thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, as well as pharmaceutical compns. comprising the compds. and methods for using the compds. and the pharmaceutical compns. for the treatment and/or prevention of sodium channel-mediated diseases or conditions, e.g. pain cardiovascular diseases, respiratory diseases, etc. Preparation of e.g. 3-chloro-N-[3-(10,11-dihydro-5H-dibenzo[a,d][7]annulen-5-ylidene)propyl]-N-methylthiophene-2-carboxamide is described.
- CC 1-12 (Pharmacology)
- ST tricyclic compd sodium channel disease treatment; sodium channel pain treatment tricyclic compd; cardiovascular respiratory disease treatment tricyclic compd; dibenzoannulenylidene deriv prepn sodium channel disease treatment
- IT Anti-AIDS agents
Antiviral agents
Drug toxicity
(HIV treatment-induced neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.7; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.8; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.9; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.2; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.4; tricyclic compds. for treatment of sodium channel-mediated diseases)

- IT Voltage-gated sodium channels
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(Nav1.5; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Antiarteriosclerotics
(antiatherosclerotics; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Prostate gland disease
(benign hyperplasia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Neoplasm
(cancer pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Central nervous system
(centrally mediated pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache
(chronic, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
(chronic; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
(diabetic neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Viscera
(disease, pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nervous system, disease
(dystonia, paroxysmal; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal
(eudynia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal
(familial erythralgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Rectum
(familial rectal pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease
(fibromyalgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Temperature effects, biological
(heat, heat sensitivity; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
(inflammatory pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Fever and Hyperthermia
(malignant; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache
(migraine, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal
(myasthenia syndromes; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease

- (myotonia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nervous system, disease
 - (neural trauma; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
 - Pain
 - (neuralgia, post-herpetic; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Bladder disease
 - (neurogenic bladder pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
 - (neuropathic pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
 - (neuropathy, HIV treatment-induced neuropathy; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
 - (neuropathy, peripheral; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Surgery
 - (pain associated with or after; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Chemotherapy
 - Human immunodeficiency virus
 - Multiple sclerosis
 - Parturition
 - Ulcerative colitis
 - (pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Seizures
 - (partial and general tonic seizures; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Nerve, disease
 - (peripheral nerve injury; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Injury
 - (peripheral nerve; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Peripheral nervous system
 - (peripherally mediated pain; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
 - (persistent; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Pain
 - (phantom limb; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Disease, animal
 - (primary erythralgia; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Aldosteronism
 - (pseudoaldosteronism; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Leg, disease
 - Sleep disorders
 - (restless leg syndrome; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Muscle, disease

- (rhabdomyolysis; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache
 - (sinus, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Toxins
 - RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (sodium channel toxin-related illnesses; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Sodium channels
 - RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (sodium channel toxin-related illnesses; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Headache
 - (tension, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Injury
 - (trauma, pain associated with; tricyclic compds. for treatment of sodium channel-mediated diseases)
- IT Amyotrophic lateral sclerosis
 - Analgesics
 - Anti-ischemic agents
 - Antiarrhythmics
 - Antiarthritics
 - Anticholesteremic agents
 - Anticonvulsants
 - Antidepressants
 - Antifibrotic agents
 - Antipsychotics
 - Antirheumatic agents
 - Antitumor agents
 - Anxiety
 - Anxiolytics
 - Arthritis
 - Atherosclerosis
 - Atrial fibrillation
 - Bipolar disorder
 - Cardiac arrhythmia
 - Cardiovascular agents
 - Cardiovascular disease
 - Crohn disease
 - Cystic fibrosis
 - Cytotoxic agents
 - Depression
 - Dermatological agents
 - Epilepsy
 - Gastrointestinal agents
 - Human
 - Hypercholesterolemia
 - Hypothyroidism
 - Irritable bowel syndrome
 - Ischemia
 - Mental and behavioral disorders
 - Neoplasm
 - Nervous system agents
 - Neuroprotective agents
 - Osteoarthritis
 - Pain
 - Prodrugs

Prophylaxis
 Pruritus
 Psychotropics
 Respiratory system agents
 Respiratory system disease
 Rheumatoid arthritis
 Sarcoidosis
 Schizophrenia
 Sodium channel blockers
 Stroke
 Tachycardia
 Ventricular fibrillation
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Voltage-gated sodium channels
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Nerve, disease
 Pain
 (trigeminal neuralgia; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Disease, animal
 (visceral pain; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT Pain
 (visceral; tricyclic compds. for treatment of sodium channel-mediated diseases)

IT 57-88-5, Cholesterol, biological studies
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

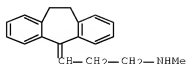
IT 1067431-34-8P 1067431-37-1P 1067431-40-6P 1067431-43-9P
 1067431-46-2P 1067431-49-5P 1067431-52-0P 1067431-55-3P
 1067431-58-6P 1067431-61-1P 1067431-64-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

IT 72-69-5 59337-89-2
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

IT 72-69-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (tricyclic compds. for treatment of sodium channel-mediated diseases)

RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)

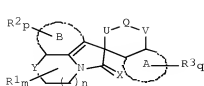


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

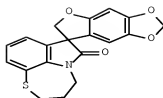
L91 ANSWER 7 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2008:473340 ZCAPLUS Full-text
 DOCUMENT NUMBER: 148:472085
 TITLE: Preparation of tricyclic spiro-oxindole derivatives
 use as therapeutic agents
 INVENTOR(S): Chafeev, Mikhail; Chowdhury, Sultan; Fu, Jianmin;
 Kamboj, Rajender
 PATENT ASSIGNEE(S): Xenon Pharmaceuticals Inc., Can.
 SOURCE: PCT Int. Appl., 138 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008046046	A1	20080417	WO 2007-US81240	20071012
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM AU 2007307635 A1 20080417 AU 2007-307635 20071012 CA 2666136 A1 20080417 CA 2007-2666136 20071012 EP 2076518 A1 20090708 EP 2007-844222 20071012 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR MX 2009003874 A 20090422 MX 2009-3874 20090408 CN 101522685 A 20090902 CN 2007-80037642 20090408 IN 2009DN02456 A 20090619 IN 2009-DN2456 20090415 PRIORITY APPLN. INFO.: US 2006-851190P P 20061012 WO 2007-US81240 W 20071012				

OTHER SOURCE(S): MARPAT 148:472085
 GI



I



II

AB Title compds. represented by the formula I [wherein U = (CH₂)_k; V = (CH₂)_j; j, k, p = independently 0-3; q = 1-4; m = 0-2; n = 0-4; Q = O, amino, SO, etc.; X = O or S; ring A = fused (hetero)aryl or fused heterocyclyl; ring B = fused (hetero)aryl or fused heterocyclyl; Y = CO, O, CF₂, etc.; R₁ = independently halo, alkyl, aryl, etc.; R₂ = independently H, halo, alkyl, etc.; R₃ = independently H, (halo)alkyl, alkynyl, etc.; and stereoisomers, enantiomers, tautomers thereof or mixts. thereof; or pharmaceutically acceptable salts, solvates or prodrugs thereof] were prepared as sodium-channel blockers. For example, II was provided in a multi-step synthesis starting from 2,3,4,5-tetrahydrobenzo[b][1,4]thiazepine. I were tested in guanidine influx assay, and other biol. assay methods were described as well. Thus, I and their pharmaceutical compns. are useful for the treatment and/or prevention of sodium channel-mediated diseases or conditions, such as pain.

CC 28-22 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

ST tricyclic spiro oxindole prepn sodium channel blocker pain treatment

IT Pain

(HIV; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(acute, eudynia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Antiarteriosclerotics

(antiatherosclerotics; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(associated with multiple sclerosis; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Prostate gland disease

(benign hyperplasia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(cancer; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(centrally mediated; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(chemotherapy; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Pain

(childbirth; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

IT Headache

Pain

(chronic; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)

- IT Nerve, disease
(diabetic neuropathy; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Viscera
(disease, pain; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Nervous system, disease
(dystonia, paroxysmal; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Skin, disease
(erythroderma, familial; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Skin, disease
(erythroderma, primary; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(familial rectal; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Muscle, disease
(fibromyalgia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(inflammatory pain; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Voltage-gated sodium channels
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(labor; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Fever and Hyperthermia
(malignant; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Headache
(migraine; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Neuromuscular transmission
(myasthenia syndromes, disorders of; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Muscle, disease
(myotonia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Bladder disease
(neurogenic; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(neuropathic pain; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Nerve, disease
(neuropathy, HIV treatment induced; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Seizures
(partial and general tonic; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Nerve, disease
(peripheral nerve injury; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Injury
(peripheral nerve; preparation of tricyclic spiro-oxindole derivs.

- use as therapeutic agents)
- IT Pain
 - (peripherally mediated; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
 - (persistent; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Headache
 - (phantom limb; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
 - (post-surgical; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Nerve, disease
 - Pain
 - (postherpetic neuralgia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Amyotrophic lateral sclerosis
- Analgesics
- Antiarrhythmics
- Antiarthritics
- Anticholesteremic agents
- Anticonvulsants
- Antidepressants
- Antipsychotics
- Antirheumatic agents
- Antitumor agents
- Anxiety
- Anxiolytics
- Atherosclerosis
- Atrial fibrillation
- Bipolar disorder
- Cardiac arrhythmia
- Cardiovascular disease
- Crohn disease
- Cystic fibrosis
- Depression
- Epilepsy
- Human
- Hypercholesterolemia
- Hypothyroidism
- Irritable bowel syndrome
- Mental and behavioral disorders
- Neoplasm
- Osteoarthritis
- Pain
- Peripheral nervous system disease
- Pruritus
- Respiratory system disease
- Rheumatoid arthritis
- Schizophrenia
- Tachycardia
- Ulcerative colitis
- Ventricular fibrillation
 - (preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Aldosteronism
 - (pseudoaldosteronism; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Leg, disease

- Sleep disorders
(restless leg syndrome; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Muscle, disease
(rhabdomyolysis; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Heat
(sensitivity; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Headache
(sinus; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Disease, animal
(sodium channel toxin related; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(surgical; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Headache
(tension; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(trauma; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Nerve, disease
Pain
(trigeminal neuralgia; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Neuroprotective agents
(under ischemic conditions caused by stroke or neural trauma; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- of
- IT Disease, animal
(visceral pain; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT Pain
(visceral; preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT 1019847-67-6P 1019847-68-7P 1019847-70-1P 1019847-71-2P
1019847-72-3P 1019847-73-4P 1019847-74-5P 1019847-75-6P
1019847-76-7P 1019847-77-8P 1019847-78-9P 1019847-79-0P
1019847-80-3P
RL: PAC (Pharmacological activity); PRPH (Prophetic); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT 1019847-61-0P 1019847-63-2P 1019847-65-4P 1019847-66-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT 533-31-3, 1,3-Benzodioxol-5-ol 7124-93-8,
1,2,3,4,5,6-Hexahydro-1-benzazocine 7160-97-6 32281-97-3,
7-Bromo-3,4-dihydronaphthalen-1(2H)-one 40358-33-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tricyclic spiro-oxindole derivs. use as therapeutic agents)
- IT 205584-61-8P 885953-12-8P 1019847-81-4P 1019847-82-5P

1019847-83-6P 1019847-86-9P 1019847-87-0P 1019847-88-1P
 1019847-89-2P 1019847-91-6P 1019847-93-8P 1019847-94-9P
 1019847-95-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of tricyclic spiro-oxindole derivs. use as
 therapeutic agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 8 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:439128 ZCAPLUS Full-text

DOCUMENT NUMBER: 149:6518

TITLE: Ceramide accumulation mediates inflammation, cell

death and infection susceptibility in cystic fibrosis

AUTHOR(S): Teichgraber, Volker; Ulrich, Martina; Endlich,
 Nicole; Riethmüller, Joachim; Wilker, Barbara; De
 Oliveira-Munding, Cheyla Conceicao; van Heeckeren,
 Anna M.; Barr, Mark L.; von Kuerthy, Gabriele; Schmid,
 Kurt W.; Weller, Michael; Tuemmler, Burkhard; Lang,
 Florian; Grassme, Heike; Doering, Gerd; Gulbins, Erich
 CORPORATE SOURCE: Department of Molecular Biology, University of
 Duisburg-Essen, Essen, 45122, Germany

SOURCE: Nature Medicine (New York, NY, United States) (2008),
 14(4), 382-391

CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Microbial lung infections are the major cause of morbidity and mortality in
 the hereditary metabolic disorder cystic fibrosis, yet the mol. mechanisms
 leading from the mutation of cystic fibrosis transmembrane conductance
 regulator (CFTR) to lung infection are still unclear. Here, we show that
 ceramide age-dependently accumulates in the respiratory tract of uninfected
 Cftr-deficient mice owing to an alkalization of intracellular vesicles in
 Cftr-deficient cells. This change in pH results in an imbalance between acid
 sphingomyelinase (Asm) cleavage of sphingomyelin to ceramide and acid
 ceramidase consumption of ceramide, resulting in the higher levels of
 ceramide. The accumulation of ceramide causes Cftr-deficient mice to suffer
 from constitutive age-dependent pulmonary inflammation, death of respiratory
 epithelial cells, deposits of DNA in bronchi and high susceptibility to severe
 Pseudomonas aeruginosa infections. Partial genetic deficiency of Asm in Cftr-
 /-Smpd1+/- mice or pharmacol. treatment of Cftr-deficient mice with the Asm
 blocker amitriptyline normalizes pulmonary ceramide and prevents all pathol.
 findings, including susceptibility to infection. These data suggest
 inhibition of Asm as a new treatment strategy for cystic fibrosis.

CC 14-4 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

ST ceramide inflammation infection susceptibility cystic fibrosis

IT Cystic fibrosis

Human

Pneumonitis

Pseudomonas aeruginosa

Respiratory system

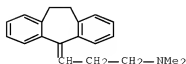
(ceramide accumulation mediates inflammation, cell death and infection
 susceptibility in cystic fibrosis)

IT CFTR (cystic fibrosis transmembrane
 conductance regulator)

Ceramides

RL: ADV (Adverse effect, including toxicity); BSU (Biological study,

- unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Sphingomyelins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT DNA
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(deposits in respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Respiratory system
(epithelium, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Apoptosis
(of respiratory epithelium; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Epithelium
(respiratory tract, cell death; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT Organelle
(vesicle, alkalinization of; ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 57-88-5, Cholesterol, biological studies 123-78-4, Sphingosine 9031-54-3, Acid sphingomyelinase 26993-30-6, Sphingosine 1-phosphate 37289-06-8, Acid ceramidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 212059-03-5, Peptamen
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- IT 50-48-6, Amitriptyline
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ceramide accumulation mediates inflammation, cell death and infection susceptibility in cystic fibrosis)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 9 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:1064527 ZCAPLUS Full-text
 DOCUMENT NUMBER: 147:371991
 TITLE: Preparation and storage of stable, biologically active materials
 INVENTOR(S): Manders, Ernest K.; Manders, Christian D.
 PATENT ASSIGNEE(S): Promethean Lifesciences, Inc., USA
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106582	A2	20070920	WO 2007-US6592	20070315
WO 2007106582	A3	20071122		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRIORITY APPLN. INFO.: US 2006-782420P P 20060315

AB The invention involves taking a base material such as allografts, xenografts, polymers, metals, and ceramics and combining it with a biol. active agent, such as proteins, cytokines, growth factors, and enzymes after which it is irradiated with ionizing radiation to sterilize and stabilize the material. The resulting biol. active material may then be stored at ambient temperature while maintaining its biol. activity and the structural integrity of the base material. The invention is particularly useful for eliciting desired biol. responses in human and animal medicine, and in certain industrial applications.

IC ICM A61K

CC 63-8 (Pharmaceuticals)

IT Actins

Albumins

Amyloid

Antibodies and Immunoglobulins

Barbiturates

Bone morphogenetic protein 11

Bone morphogenetic proteins

C-reactive protein

CFTR (cystic fibrosis transmembrane
conductance regulator)

Cadherins

Chemokines

Cholinergic receptors
 Collagens
 Cytokines
 Dystrophin
 Elastins
 Enzymes
 Eotaxins
 Estrogen receptors
 Ferritins
 Fetuins
 Fibrins
 Gelatins
 Glucose transporters
 Glycosaminoglycans
 Growth factors, animal
 Hemoglobins
 Hepatocyte growth factor
 Histones
 Hormones, animal
 Insulin receptors
 Integrins
 Interferons
 Interleukin receptors
 Interleukins
 Keratins
 Leukemia inhibitory factor
 Macrophage inflammatory protein 1 α
 Macrophage inflammatory protein 1 β
 Macrophage inflammatory protein 3 β
 Macrophage inflammatory protein 4
 Macrophage inflammatory proteins
 Metals
 Monocyte chemoattractant proteins
 Myoglobins
 Myosins
 Neuregulin 1
 Neuregulin 1
 Peptides
 Platelet-derived growth factors
 Polymers
 Polysaccharides
 Potassium channels
 Protein C
 Proteins
 RANTES (chemokine)
 Rennets
 Selectins
 Stem cell factor
 Steroids
 T cell receptors
 Tau proteins
 Thioredoxins
 Toxins
 Toxins
 Transforming growth factors
 Tubulins
 Tumor necrosis factors
 p53 (protein)
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (preparation and storage of stable, biol. active materials)
- II 50-06-6, Phenobarbital, biological studies 50-24-8, Prednisolone
 50-33-9, Phenylbutazone, biological studies 50-48-6,
 Amitriptyline 50-53-3, Chlorpromazine, biological studies 50-55-5,
 Reserpine 50-56-6, Oxytocin, biological studies 50-78-2, Aspirin
 51-06-9, Procainamide 51-43-4, Epinephrine 51-55-8, Atropine,
 biological studies 57-42-1, Meperidine 57-47-6, Physostigmine
 57-53-4, Meprobamate 58-22-0, Testosterone 58-39-9, Perphenazine
 58-55-9, Theophylline, biological studies 58-73-1, Diphenhydramine
 58-74-2, Papaverine 58-94-6, Chlorothiazide 59-42-7, Phenylephrine
 59-47-2, Nephrenesin 59-99-4, Neostigmine 69-23-8, Fluphenazine
 72-69-5, Mornitriptyline 73-48-3, Bendroflumethiazide 76-99-3,
 Methadone 77-21-4, Glutethimide 91-81-6, Tripeleminine 103-90-2,
 Acetaminophen 146-54-3, Triflupromazine 148-56-1, Flumethiazide
 299-42-3, Ephedrine 302-17-0, Chloral hydrate 409-21-2, Silicon
 carbide, biological studies 469-62-5, Propoxyphene 523-87-5,
 Dimenhydrinate 525-66-6, Propranolol 1302-88-1, Cordierite
 1314-23-4, Zirconia, biological studies 1344-28-1, Alumina, biological
 studies 1398-61-4, Chitin 5818-17-7, Methanthelone 7440-06-4,
 Platinum, biological studies 7440-09-7, Potassium, biological studies
 7440-22-4, Silver, biological studies 7440-32-6, Titanium, biological
 studies 7440-57-5, Gold, biological studies 7632-10-2, Deoxyephedrine
 9000-69-5, Pectin 9000-83-3, ATPase 9000-86-6, Alanine transaminase
 9000-92-4, Amylase 9000-96-8, Arginase 9000-97-9 9001-03-0, Carbonic
 anhydrase 9001-05-2, Catalase 9001-06-3, Chitinase 9001-08-5,
 Cholinesterase 9001-15-4, Creatine kinase 9001-16-5, Cytochrome c
 oxidase 9001-25-6, Blood-coagulation factor VII 9001-28-9, Factor IX
 9001-29-0, Blood-coagulation factor X 9001-30-3, Blood-coagulation
 factor XII 9001-37-0, Glucose oxidase 9001-42-7, Maltase 9001-48-3,
 Glutathione reductase 9001-50-7, Glyceraldehyde 3-phosphate
 dehydrogenase 9001-51-8, Hexokinase 9001-52-9, Fructose bisphosphatase
 9001-54-1, Hyaluronidase 9001-58-5, Isocitrate dehydrogenase
 9001-60-9, Lactate dehydrogenase 9001-63-2, Lysozyme 9001-64-3, Malate
 dehydrogenase 9001-66-5, Monoamine oxidase 9001-69-8, Ornithine
 transcarbamoylase 9001-75-6, Pepsin 9001-78-9, Alkaline phosphatase
 9001-80-3, Phosphofructokinase 9001-81-4, Phosphoglucosutase
 9001-90-5, Plasmin 9001-99-4 9002-03-3, Dihydrofolate reductase
 9002-04-4, Thrombin 9002-06-6, Thymidine kinase 9002-07-7, Trypsin
 9002-08-8, Trypsinogen 9002-10-2, Catechol oxidase 9002-12-4, Urate
 oxidase 9002-13-5, Urease 9002-17-9, Xanthine oxidase 9003-98-9,
 Deoxyribonuclease 9003-99-0, Myeloperoxidase 9004-02-8, Lipoprotein
 lipase 9004-06-2, Elastase 9004-07-3, Chymotrypsin 9004-10-8,
 Insulin, biological studies 9004-32-4, Carboxymethyl cellulose
 9004-57-3, Ethyl cellulose 9004-62-0, Hydroxyethyl cellulose
 9004-64-2, Hydroxypropyl cellulose 9005-38-3, Algin 9005-49-6,
 Heparin, biological studies 9012-25-3, Catechol-O-methyl transferase
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 9012-76-4, Chitosan 9012-78-6, Choline acetyltransferase 9012-90-2,
 DNA polymerase 9013-02-9, Adenylate kinase 9013-04-1, Nitrogenase
 9013-55-2, Blood-coagulation factor XI 9013-56-3, Factor XIII
 9013-66-5, Glutathione peroxidase 9013-93-8, Phospholipase 9014-19-1,
 Pyruvate carboxylase 9014-20-4, Pyruvate dehydrogenase 9014-42-0,
 Thrombopoietin 9014-52-2, Tryptophan synthase 9015-82-1,
 Angiotensin-converting enzyme 9015-94-5, Renin, biological studies
 9016-11-9, Galactose-1-phosphate uridylyltransferase 9016-12-0,
 Hypoxanthine-guanine phosphoribosyltransferase 9023-56-7, CTP synthase
 9023-58-9, Argininosuccinate synthetase 9023-93-2, Acetyl-CoA
 carboxylase 9024-60-6, Ornithine decarboxylase 9024-78-6, Kynureninase
 9024-90-2, Nitrilase 9026-81-7, Nuclease 9026-93-1, Adenosine
 deaminase 9027-03-6, Coenzyme Q-cytochrome c reductase 9027-23-0,

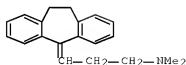
RubisCO 9027-41-2, Hydrolase 9028-13-1, Homoserine dehydrogenase 9028-14-2, Glycerol dehydrogenase 9028-15-3, Propanediol phosphate dehydrogenase 9028-16-4, D-Xylulose reductase 9028-17-5, L-Xylulose reductase 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 9028-49-3, Diacetyl reductase 9028-69-7, Methylenetetrahydrofolate reductase 9028-78-8, L-Gulonolactone oxidase 9028-86-8, Acetaldehyde dehydrogenase 9029-22-5, Sarcosine oxidase 9029-38-3, Sulfite oxidase 9029-53-2, Cytochrome c peroxidase 9029-72-5, 4-Hydroxyphenylpyruvate dioxygenase 9029-73-6, Phenylalanine hydroxylase 9030-23-3, Platelet derived endothelial cell growth factor 9030-35-7, Thiaminase 9031-11-2, Lactase 9031-28-1, Thyroid peroxidase 9031-37-2, Ceruloplasmin 9031-44-1, Kinase (phosphorylating) 9031-72-5, Alcohol dehydrogenase 9034-39-3, Growth Hormone Releasing Factor 9035-82-9, Dehydrogenase 9037-14-3, Aminolevulinic acid synthase 9037-42-7 9039-48-9, Aromatase 9042-64-2, Aromatic-L-amino acid decarboxylase 9046-27-9 9046-38-2, Polygalacturonic acid 9054-63-1, Alanine aminopeptidase 9054-75-5, Guanylate cyclase 9054-89-1, Superoxide dismutase 9055-11-2 9057-02-7, Pullulan 9061-61-4, Nerve growth factor 9067-75-8, Blood-coagulation factor XIIIa 9068-38-6, Reverse transcriptase 9068-57-9, Acrosin 9073-60-3 9074-10-6, Biliverdin reductase 9074-14-0, Thioredoxin reductase 9075-08-5 9075-42-7, Cytochrome P450 oxidase 9075-65-4, Glycerol-3-phosphate dehydrogenase 9076-80-6 9079-67-8 9081-34-9, 5- α Reductase 11096-26-7, Erythropoietin 11100-70-2, Vanadium steel, biological studies 12033-89-5, Silicon nitride, biological studies 12597-68-1, Stainless steel, biological studies 12683-48-6 14378-12-2, Stearate 25249-06-3, Polygalacturonic acid 37205-63-3, ATP synthase 37228-74-3 37250-13-8 37259-58-8 37270-94-3, Platelet factor 4 37288-39-4 37289-19-3, GTP cyclohydrolase I 37318-49-3, Protein disulfide isomerase 42200-33-9, Nadolol 49557-75-7 50812-37-8, Glutathione S-transferase 52013-44-2 53986-32-6, Protoporphyrinogen oxidase 57285-09-3, Inhibin 60202-16-6, Protein C 61869-41-8, Renilla luciferase 61912-98-9, Insulin-like growth factor 61969-99-1, Cypridina luciferase 61970-00-1, Firefly luciferase 62031-54-3, Fibroblast growth factor 62213-29-0 62229-50-9, Epidermal growth factor 62571-86-2, Captopril 62683-29-8, Colony-stimulating factor 63774-49-2 64885-96-7, Primase 72103-04-9, Deiodinase 73200-91-6, DMSO reductase 74870-74-9, Uridine monophosphate synthase 75847-73-3, Enalapril 80449-02-1 80498-15-3, Laccase 81669-70-7 86480-67-3, Ubiquitin carboxyterminal hydrolase 106956-32-5, Oncostatin M 114051-83-1, Dihydrobenzophenanthridine oxidase 117147-70-3, Amphiregulin 125978-95-2 127464-60-2, Vascular endothelial growth factor 139639-23-9, Tissue plasminogen activator 141907-41-7 142008-29-5, CAMP-dependent protein kinase 148348-15-6, Fibroblast growth factor 7 154531-34-7, HB-EGF 154947-66-7, LL-37 163150-12-7, Betacellulin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and storage of stable, biol. active materials)

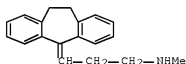
IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and storage of stable, biol. active materials)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS
 CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



L91 ANSWER 10 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:605195 ZCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 145:83360
 TITLE: Novel heterocyclic compounds, their preparation, and their use as PDE4 inhibitors for treating inflammatory and allergic disorders
 INVENTOR(S): Gharat, Laxmikant Atmaram; Gopalan, Balasubramanian; Khairatkar-Joshi, Neelima
 PATENT ASSIGNEE(S): Glenmark Pharmaceuticals S.A., Switz.
 SOURCE: PCT Int. Appl., 145 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006064355	A2	20060622	WO 2005-IB3798	20051215
WO 2006064355	A3	20060803		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005315319	A1	20060622	AU 2005-315319	20051215
CA 2591438	A1	20060622	CA 2005-2591438	20051215
EP 1831227	A2	20070912	EP 2005-826587	20051215

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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BA, HR, MK, YU

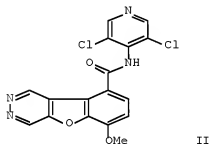
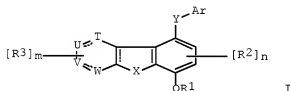
JP 2008524201	T	20080710	JP 2007-546221	20051215
BR 2005017211	A	20080930	BR 2005-17211	20051215
MX 2007007345	A	20070907	MX 2007-7345	20070618
KR 2007100254	A	20071010	KR 2007-714219	20070622
NO 2007003436	A	20070905	NO 2007-3436	20070703
ZA 2007006097	A	20080730	ZA 2007-6097	20070713
IN 2007MN01058	A	20090522	IN 2007-MN1058	20070713
CN 101124229	A	20080213	CN 2005-80048315	20070814

PRIORITY APPLN. INFO.:

IN 2004-MU1352	A	20041217
US 2004-637232P	P	20041217
WO 2005-IB3798	W	20051215

OTHER SOURCE(S): CASREACT 145:83360; MARPAT 145:83360

GI



AB The invention is related to novel phosphodiesterase type 4 (PDE4) inhibitors of the formula I [R1-R3 at each occurrence = independently H, OH, CN, halo, (un)substituted alk(en/yn)yl, hetero/aryl, NH2 and derivs., etc.; Ar = (un)substituted hetero/aryl, hetero/arylalkyl, heterocyclyl, heterocycloalkyl; m = 0-8; n = 0-2; T, U, V, W = independently C, C:O, N, NH and derivs., O, S, with the proviso that at least one of T, U, V, and W are N, NH and derivs., O, or S; X = O, S, SO, SO2, NH and derivs.; Y = CONH and derivs., NHSO2 and derivs., SO2NH and derivs., NHC(O), and derivs.] and analogs, tautomers, enantiomers, diastereomers, regioisomers, stereoisomers, polymorphs, pharmaceutically acceptable salts, N-oxides, pharmaceutically acceptable solvates thereof, their preparation, and the pharmaceutical compns. containing them which are useful in the treatment of allergic (no data), inflammatory (no data), central nervous system diseases (no data) and insulin-resistant diabetes (no data). For example, II was prepared in 13 steps via cyclization of 2-Et 4-Me 3-formyl-7-methylbenzo[b]furan-2,4-dicarboxylate with hydrazine hydrate, followed by aromatization with POCl3 to 4-chlorobenzofuroprydazine derivative, dechlorination, saponification of the ester, esterification with p-nitrophenol, and reaction with 4-amino-3,5-dichloropyridine. II inhibited the PDE4-induced conversion of [3H]cAMP to the corresponding [3H]5'-AMP with IC50 of 1.375 nM. Thus, I and their compns., are useful for treating

- including asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, psoriasis, rheumatoid arthritis, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and reperfusion injury of the brain, chronic glomerulonephritis, endotoxic shock, adult respiratory distress syndrome, etc. (no data).
- CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
- IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1, secretion; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation
(Crohn's disease; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Intestine, disease
(Crohn's; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Respiratory distress syndrome
(adult; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy
Inflammation
Nose, disease
(allergic rhinitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Dermatitis
(atopic; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Muscle
(cardiac, reperfusion injury of; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Brain, disease
(cerebrovascular; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Bronchi, disease
Inflammation
(chronic bronchitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation
Kidney, disease
(chronic glomerulonephritis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Lung, disease

- (chronic obstructive pulmonary disease; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation
(chronic; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye, disease
Inflammation
(conjunctivitis, adult vernal; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Mental and behavioral disorders
(dementia; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Mental and behavioral disorders
(depression; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Granuloma
(eosinophilic; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Heart, disease
(failure; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye
Heart
Intestine
Joint, anatomical
Lung
Skin
(inflammatory condition or immune disorder of; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Intestine, disease
(inflammatory; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Reperfusion
(injury, of myocardium and brain; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Diabetes mellitus
(insulin-resistant; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Heart
(myocardium, reperfusion injury of; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Inflammation
Kidney, disease
(nephritis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Allergy

Allergy inhibitors
 Alzheimer's disease
 Amnesia
 Anti-Alzheimer's agents
 Anti-inflammatory agents
 Antiarthritics
 Antiasthmatics
 Antidepressants
 Antidiabetic agents
 Antirheumatic agents
 Asthma
 Bronchodilators
 Cardiovascular agents
 Central nervous system, disease
 Central nervous system agents
 Cystic fibrosis
 Drug delivery systems
 Eczema
 Gout
 Human
 Immune disease
 Immunomodulators
 Inflammation
 Multiple sclerosis
 Osteoarthritis
 Psoriasis
 Psychotropics
 Respiratory distress syndrome
 Rheumatic diseases
 Shock (circulatory collapse)
 Urticaria
 (preparation of tricyclic heterocycles as PDE4 inhibitors for
 treating inflammatory, immune and central nervous system disorders, and
 insulin-resistant diabetes)
 IT Tricyclic compounds
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of tricyclic heterocycles as PDE4 inhibitors for
 treating inflammatory, immune and central nervous system disorders, and
 insulin-resistant diabetes)
 IT Brain
 (reperfusion injury of; preparation of tricyclic heterocycles as
 PDE4 inhibitors for treating inflammatory, immune and central nervous
 system disorders, and insulin-resistant diabetes)
 IT Injury
 (reperfusion, of myocardium and brain; preparation of tricyclic
 heterocycles as PDE4 inhibitors for treating inflammatory, immune and
 central nervous system disorders, and insulin-resistant diabetes)
 IT Shock (circulatory collapse)
 (septic; preparation of tricyclic heterocycles as PDE4 inhibitors
 for treating inflammatory, immune and central nervous system disorders,
 and insulin-resistant diabetes)
 IT Inflammation
 Spinal column, disease
 (spondylitis, rheumatoid; preparation of tricyclic heterocycles as
 PDE4 inhibitors for treating inflammatory, immune and central nervous
 system disorders, and insulin-resistant diabetes)
 IT Inflammation
 Intestine, disease

- (ulcerative colitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT Eye, disease
Inflammation
(uveitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 893554-81-9P 893555-11-8P 893555-23-2P 893555-31-2P 893555-43-6P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-methyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-51-6P 893555-74-3P 893555-90-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 893554-82-2P 893554-99-9P 893555-22-1P 893555-34-5P 893555-35-6P 893555-49-2P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-benzyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-50-5P, tert-Butyl 9-[(3,5-dichloropyridin-4-yl)carbamoyl]-6-methoxy-5-cyclopropylmethyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-52-7P 893555-53-8P 893555-54-9P 893555-55-0P, tert-Butyl 9-[(pyridin-4-yl)carbamoyl]-6-methoxy-5-methyl-1,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole-2-carboxylate 893555-56-1P 893555-57-2P 893555-61-8P 893555-64-1P 893555-68-5P 893555-88-9P 893555-89-0P 893555-91-4P 893555-92-5P 893555-96-9P 893556-00-8P 893556-04-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 9036-21-9, PDE4
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (insulin-resistant diabetes; preparation of tricyclic heterocycles as PDE4 inhibitors for treating inflammatory, immune and central nervous system disorders, and insulin-resistant diabetes)
- IT 18703-79-2P, Ethyl 2-(2-methoxyphenoxy)-3-oxobutanoate 18703-82-7P, Ethyl 7-methoxy-3-methylbenzo[b]furan-2-carboxylate 29025-30-7P, 7-Methoxy-2-methylbenzo[b]furan 39581-47-0P, (7-Methoxybenzo[b]furan-3-yl)acetonitrile 41580-71-6P, 1-Methoxy-2-(2-propynyloxy)benzene 50551-58-1P 70076-67-4P, Ethyl 2-(2-formyl-6-methoxyphenoxy)acetate 75566-54-0P, (7-Methoxybenzo[b]furan-2-yl)methanol 75566-55-1P, 2-(Chloromethyl)-7-methoxy-1-benzofuran 75566-56-2P, (7-Methoxybenzo[b]furan-2-yl)acetonitrile 91872-02-5P, 4-Amino-3,5-dichloropyridine N-oxide 130627-28-0P, 7-Methoxy-2-methylbenzo[b]furan-4-carboxaldehyde 203575-64-8P, 7-Methoxy-2-methylbenzo[b]furan-4-carboxylic acid 206761-96-8P, Ethyl 4-[(2-methoxyphenyl)sulfanyl]-3-oxobutanoate 893554-82-0P, Ethyl 4-formyl-7-methoxy-3-methylbenzo[b]furan-2-carboxylate 893554-83-1P, 2-Ethoxycarbonyl-7-methoxy-3-methylbenzo[b]furan-4-carboxylic acid

893554-84-2P 893554-85-3P 893554-86-4P 893554-87-5P 893554-88-6P
 893554-89-7P 893554-90-0P 893554-91-1P 893554-93-3P, Ethyl
 2-(2-cyano-6-methoxyphenoxy)acetate 893554-94-4P 893554-95-5P
 893554-96-6P 893554-97-7P 893554-98-8P 893555-00-5P, Methyl
 7-methoxy-2-methylbenzo[b]furan-4-carboxylate 893555-01-6P, Methyl
 2-bromomethyl-7-methoxybenzo[b]furan-4-carboxylate 893555-02-7P, Methyl
 2-formyl-7-methoxybenzo[b]furan-4-carboxylate 893555-03-8P,
 (Z)-3-[(7-Methoxy-4-[(methyloxy)carbonyl]benzo[b]furan-2-yl]-2-propenoic
 acid 893555-04-9P, Methyl 2-[(Z)-2-(azidocarbonyl)ethenyl]-7-
 methoxybenzo[b]furan-4-carboxylate 893555-05-0P 893555-06-1P
 893555-07-2P 893555-08-3P 893555-09-4P 893555-10-7P 893555-12-9P,
 2-Ethoxycarbonyl-7-hydroxy-3-methylbenzo[b]furan-4-carboxylic acid
 893555-13-0P 893555-14-1P 893555-15-2P, Diethyl
 3-bromomethyl-7-difluoromethoxybenzo[b]furan-2,4-dicarboxylate
 893555-16-3P, Diethyl 7-difluoromethoxy-3-formylbenzo[b]furan-2,4-
 dicarboxylate 893555-17-4P 893555-18-5P 893555-19-6P 893555-20-9P
 893555-21-0P 893555-24-3P, Ethyl
 2-(7-methoxybenzo[b]thiophen-3-yl)acetate 893555-25-4P,
 2-(7-Methoxybenzo[b]thiophen-3-yl)acetamide 893555-26-5P,
 [2-(7-Methoxybenzo[b]thiophen-3-yl)ethyl]amine 893555-27-6P, Ethyl
 [2-(7-methoxybenzo[b]thiophen-3-yl)ethyl]carbamate 893555-32-3P
 893555-33-4P 893555-36-7P, 2-(7-Methoxybenzo[b]furan-2-yl)ethanamine
 893555-37-8P, Ethyl [2-(7-methoxybenzo[b]furan-2-yl)ethyl]carbamate
 893555-38-9P 893555-39-0P 893555-40-3P 893555-41-4P 893555-42-5P
 893555-44-7P, Methyl 3-(2-chlorohydrazino)-4-methoxybenzoate
 893555-45-8P 893555-46-9P 893555-47-0P,
 2-(tert-Butyloxycarbonyl)-6-methoxy-5-methyl-1,3,4,5-tetrahydro-2H-
 pyrido[4,3-b]indole-9-carboxylic acid 893555-48-1P 893555-58-3P,
 2-(7-Methoxybenzo[b]furan-3-yl)ethanamine hydrochloride 893555-59-4P,
 Ethyl [2-(7-methoxybenzo[b]furan-3-yl)ethyl]carbamate 893555-60-7P
 893555-62-9P 893555-63-0P 893555-65-2P 893555-66-3P 893555-67-4P
 893555-69-6P 893555-70-9P 893555-71-0P 893555-72-1P 893555-73-2P
 893555-75-4P, 7-Hydroxy-2-methylbenzo[b]furan-4-carboxaldehyde
 893555-76-5P, 7-Cyclopentyl-2-methylbenzo[b]furan-4-carboxaldehyde
 893555-77-6P, 7-Cyclopentyl-2-methylbenzo[b]furan-4-carboxylic acid
 893555-78-7P, Methyl 7-cyclopentyl-2-methylbenzo[b]furan-4-carboxylate
 893555-79-8P, Methyl 7-cyclopentyl-2-bromomethylbenzo[b]furan-4-
 carboxylate 893555-80-1P, Methyl
 2-formyl-7-(cyclopentyl)benzo[b]furan-4-carboxylate 893555-81-2P,
 (Z)-3-[(7-Cyclopentyl)oxy-4-[(methyloxy)carbonyl]benzo[b]furan-2-yl]-2-
 propenoic acid 893555-82-3P 893555-83-4P 893555-84-5P 893555-85-6P
 893555-86-7P 893555-87-8P 893555-93-6P 893555-94-7P 893555-95-8P
 893555-97-0P 893555-98-1P 893555-99-2P 893556-01-9P 893556-02-0P
 893556-03-1P 893556-05-3P 893556-06-4P 893556-07-5P 893556-08-6P
 1097718-39-2P 1097721-21-5P 1097721-58-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(intermediate; preparation of tricyclic heterocycles as PDE4
 inhibitors for treating inflammatory, immune and central nervous system
 disorders, and insulin-resistant diabetes)

IT 90-05-1, Guaiacol 100-02-7, p-Nitrophenol, reactions 105-36-2, Ethyl
 bromoacetate 106-96-7, Propargyl bromide 109-65-9, n-Butyl bromide
 137-43-9, Cyclopentyl bromide 148-53-8, o-Vanillin 372-09-8,
 Cyanoacetic acid 504-24-5, 4-Aminopyridine 621-59-0, Isovanillin
 638-07-3, Ethyl 4-chloroacetate 1073-70-7, p-Chlorophenylhydrazine
 hydrochloride 3731-16-6, 3-Carboxy-2-piperidone 7051-34-5,
 Cyclopropylmethyl bromide 7169-37-1, 7-Methoxy-1-benzofuran-3(2H)-one
 7217-59-6 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl
 4-methoxy-3-aminobenzoate 54527-68-3, 2-Chloroethyl acetoacetate
 79099-07-3, N-Boc-4-piperidone

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of tricyclic heterocycles as PDE4 inhibitors for
 treating inflammatory, immune and central nervous system disorders, and
 insulin-resistant diabetes)

IT 1027054-25-6P 1097710-58-1P 1097711-07-3P 1108149-13-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of tricyclic heterocycles as PDE4 inhibitors for
 treating inflammatory, immune and central nervous system disorders, and
 insulin-resistant diabetes)

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
 (2 CITINGS)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 11 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:318526 ZCAPLUS Full-text
 DOCUMENT NUMBER: 144:344946
 TITLE: Molecular toxicity models based on gene expression
 profiles in isolated rat hepatocytes exposed to known
 hepatotoxins

INVENTOR(S): Higgs, Brandon; Elashoff, Michael; Mendrick, Donna L.;
 Porter, Mark W.; Castle, Arthur L.; Johnson, Kory R.

PATENT ASSIGNEE(S): Gene Logic, Inc., USA

SOURCE: PCT Int. Appl., 271 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2006037025	A2	20060406	WO 2005-US34780	20050928
WO 2006037025	A3	20060713		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2004-613292P P 20040928

AB The present invention includes methods of predicting hepatotoxicity of test agents and methods of generating hepatotoxicity prediction models using algorithms for analyzing quant. gene expression information. Isolated Sprague-Dawley rat hepatocytes exposed to known hepatotoxins were examined to identify changes in genes expression induced by these compds. using the Affymetrix Rat Microarray. These changes in gene expression provide useful toxicity markers than can be used to monitor toxicity and/or toxicity progression by a test compound. Some of these markers may also be used to monitor or detect various disease or physiol. states, disease progression, drug efficacy, and drug metabolism. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.

CC 4-3 (Toxicology)
 Section cross-reference(s): 3

IT APC protein
 Agrins
 Bone morphogenetic protein 6
 C-reactive protein
 CD3 (antigen)
 CD59 (antigen)
 CFTR (cystic fibrosis transmembrane
 conductance regulator)
 Calcitonin gene-related peptide receptors
 Calnexin
 Fibronectins
 GAP-43 (protein)
 Glucagon receptors
 Gonadotropin receptors
 Growth hormone receptors
 Haptoglobin
 Hemoexins
 Insulin receptors
 Interleukin 15
 Interleukin 4 receptors
 Interleukin 6 receptors
 Intrinsic factors
 Leukemia inhibitory factor receptors
 Macrophage inflammatory protein 1a
 Metallothioneins
 Neuregulin 1
 Nicotinic receptors
 Polymeric immunoglobulin receptors
 TCR (T cell receptors)
 Tau factor
 Transferrin receptors
 Transferrins
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (mol. toxicity models based on gene expression profiles in isolated rat
 hepatocytes exposed to known hepatotoxins)

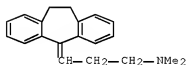
IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies
 50-48-6, Amitriptyline 50-78-2, Acetylsalicylic acid 51-61-6,
 Dopamine, biological studies 53-86-1, Indomethacin 54-85-3, Isoniazid
 55-18-5, Diethylnitrosamine 56-23-5, Carbon tetrachloride, biological
 studies 56-49-5, 3-Methylcholanthrene 57-47-6, Physostigmine
 57-63-6, 17 α -Ethinylestradiol 57-92-1, Streptomycin, biological
 studies 58-73-1, Diphenhydramine 59-05-2, Methotrexate 60-54-8,
 Tetracycline 62-44-2, Phenacetin 62-55-5, Thioacetamide 62-75-9,
 Dimethylnitrosamine 67-66-3, Chloroform, biological studies 99-66-1
 103-90-2, Acetaminophen 107-18-6, Allyl alcohol, biological studies
 108-86-1, Bromobenzene, biological studies 113-92-8, Chlorpheniramine
 maleate 298-46-4, Carbamazepine 321-64-2, Tacrine 427-51-0,
 Cyproterone acetate 551-06-4, 1-Naphthyl isothiocyanate 637-07-0,
 Clofibrate 657-24-9, Metformin 1403-66-3, Gentamicin 1951-25-3,
 Amiodarone 2764-72-9, Diquat 6621-47-2 7778-39-4, Arsenic acid
 10540-29-1, Tamoxifen 13073-35-3, L-Ethionine 13311-84-7, Flutamide
 15307-86-5, Diclofenac 22494-42-4, Diflunisal 25122-41-2, Clobetasol
 25451-15-4, Felbamate 25812-30-0, Gemfibrozil 29342-05-0, Ciclopirox
 33419-42-0, Etoposide 37148-27-9, Clenbuterol 49562-28-9, Fenofibrate
 49780-10-1, AY-25329 50892-23-4 52214-84-3, Ciprofibrate 75330-75-5,
 Lovastatin 122320-73-4, Rosiglitazone 132138-76-2, CI 1000
 393186-10-2, Compound A

RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (mol. toxicity models based on gene expression profiles in isolated rat hepatocytes exposed to known hepatotoxins)

IT 50-48-6, Amitriptyline
 RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (mol. toxicity models based on gene expression profiles in isolated rat hepatocytes exposed to known hepatotoxins)

RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



L91 ANSWER 12 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:

2005:823681 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER:

143:216704

TITLE:

Crystalline polymorphs of a CX-C-chemokine receptor ligand

INVENTOR(S):

Hu, Mengwei; Yu, Younong; Dwyer, Michael; Taveras, Arthur G.; Kim-Meade, Agnes; Yin, Jianguo; Fu, Xiaoyong; Mcallister, Timothy; Zhang, Shuyi; Klopfer, Kevin

PATENT ASSIGNEE(S):

Schering Corporation, USA

SOURCE:

PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075447	A1	20050818	WO 2005-US3414	20050128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210504	A1	20050818	AU 2005-210504	20050128
AU 2005210504	B2	20090108		
CA 2554709	A1	20050818	CA 2005-2554709	20050128
US 20050192345	A1	20050901	US 2005-45772	20050128
EP 1723131	A1	20061122	EP 2005-712748	20050128

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,
HR, LV, MK, YU

CN 1914187	A	20070214	CN 2005-80003507	20050128
BR 2005007329	A	20070703	BR 2005-7329	20050128
JP 2007519751	T	20070719	JP 2006-551613	20050128
MX 2006008599	A	20060828	MX 2006-8599	20060728
KR 2006128981	A	20061214	KR 2006-715429	20060728
KR 883476	B1	20090216		
IN 2006CN02800	A	20070608	IN 2006-CN2800	20060728
ZA 2006006295	A	20080227	ZA 2006-6295	20060728
NO 2006003841	A	20061027	NO 2006-3841	20060829
US 20080279822	A1	20081113	US 2008-174470	20080716

PRIORITY APPLN. INFO.:

US 2004-540487P	P	20040130
US 2005-45772	A1	20050128
WO 2005-US3414	W	20050128

AB The present invention relates to 4 distinct crystalline polymorphs of a monohydrate of 2-hydroxy-N,N-dimethyl-3-[[2-[[1-(5-methyl-2-furanyl)propylamino]-3,4-dioxo-1-cyclobuten-1-yl]amino]benzamide. These 4 polymorphic forms, herein referred to as Forms I, II, III and IV are active as a CXCR-chemokine receptor ligands. The invention is further directed to formulations, methods of treatment, and processes of synthesis of these polymorphic forms.

IC ICM C07D307-52
ICS A61K031-341; A61P029-00; A61P035-00

CC 63-6 (Pharmaceuticals)

IT Acne

Alzheimer's disease
Angiogenesis
Angiogenesis inhibitors
Anticoagulants
Anticonvulsants
Antidepressants
Antirheumatic agents
Antitumor agents
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Bronchodilators
Burn
Celiac disease
Common cold
Cough
Cystic fibrosis
Decongestants
Dopamine agonists
Drug delivery systems
Dyspnea
Emphysema
Encephalitis
Expectorants
Gout
Hemorrhage
Hepatitis virus
Human
Human herpesvirus
Human immunodeficiency virus 1
Hypercapnia
Immunosuppressants

Inflammation
 Ischemia
 Leukotriene antagonists
 Lupus erythematosus
 Malaria
 Meningitis
 Multiple sclerosis
 Neoplasm
 Osteoarthritis
 Osteoporosis
 Pain
 Parturition
 Platelet aggregation inhibitors
 Polymorphism (crystal)
 Pruritus
 Psoriasis
 Rheumatoid arthritis
 Sarcoidosis
 Sepsis
 Strain
 Thrombolytics
 Thrombosis

β 2-Adrenoceptor agonists

Natural products, pharmaceutical

RL: BIOL (Biological study); USES (Uses)

(crystalline polymorphs of CXC-chemokine receptor ligand)

IT 50-48-6 53-03-2, Prednisone 53-86-1, Indomethacin 59-05-2,
 Methotrexate 72-69-5 298-46-4, Carbamazepin 378-44-9,
 Betamethasone 446-86-6 599-79-1, Sulfasalazine 9005-49-6, Heparin,
 biological studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen
 22204-53-1, Naproxen 36322-90-4, Piroxicam 60142-96-3, Gabapentin
 65271-80-9 71125-38-7, Meloxicam 75706-12-6, Leflunimide 79217-60-0,
 Cyclosporin 84057-84-1, Lamotrigine 105857-23-6, Alteplase
 139639-23-9, Tissue plasminogen activator 143653-53-6, Abciximab
 147245-92-9, Glatiramer acetate 148553-50-8, Pregabalin 162011-90-7,
 Rofecoxib 169590-42-5, Celecoxib 170277-31-3, Infliximab
 181695-72-7, Valdecoxib 185243-69-0, Etanercept 188627-80-7,
 Eftifibatide 191588-94-0, Tenecteplase 202409-33-4, Etoricoxib
 331731-18-1, Adalimumab

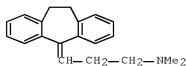
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crystalline polymorphs of CXC-chemokine receptor ligand)

IT 50-48-6 72-69-5
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (crystalline polymorphs of CXC-chemokine receptor ligand)

RN 50-48-6 ZCAPLUS

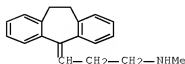
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS

10/524815

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 13 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:673292 ZCAPLUS Full-text

DOCUMENT NUMBER: 143:172866

TITLE: Preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands

INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattil J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang
 PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacoceia Drug Discovery, Inc.

SOURCE: PCT Int. Appl., 427 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068460	A1	20050728	WO 2004-US42720	20041220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MX, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2550540	A1	20050728	CA 2004-2550540	20041220
US 20060025453	A1	20060202	US 2004-17505	20041220
EP 1697354	A1	20060906	EP 2004-814856	20041220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
CN 1918156	A	20070221	CN 2004-80041794	20041220
JP 2007515489	T	20070614	JP 2006-547206	20041220
MX 2006007205	A	20060831	MX 2006-7205	20060622
PRIORITY APPLN. INFO.:			US 2003-531693P	P 20031222

OTHER SOURCE(S): CASREACT 143:172866; MARPAT 143:172866
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example preps. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazoledioxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

IC ICM C07D417-12
ICS C07D275-02; C07D417-14; A61K031-427; A61P035-00; A61P029-00

CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT AIDS (disease)
Acne
Alzheimer's disease
Analgesics
Anemia (disease)
Angiogenesis
Angiogenesis inhibitors
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-ischemic agents
Antianginal agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antimalarials
Antiphospholipid syndrome
Antirheumatic agents
Antitumor agents
Antitussives
Antiulcer agents
Antiviral agents
Arthritis
Asthma
Atherosclerosis
Behcet's syndrome
Burn
Celiac disease
Central nervous system, neoplasm
Cirrhosis
Combination chemotherapy
Common cold
Cough
Cystic fibrosis
Dermatomyositis

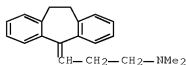
Diabetes mellitus
 Drug delivery systems
 Dyspnea
 Emphysema
 Encephalitis
 Fibrosis
 Gout
 Graves' disease
 Hepatitis virus
 Herpesviridae
 Human
 Human herpesvirus
 Human herpesvirus 8
 Hypercapnia
 Hypoxia
 Immunomodulators
 Lung, disease
 Lupus erythematosus
 Malaria
 Meningitis
 Multiple organ failure
 Multiple sclerosis
 Myasthenia gravis
 Myelodysplastic syndromes
 Myositis
 Neoplasm
 Osteoarthritis
 Osteoporosis
 Pruritus
 Psoriasis
 Respiratory system, disease
 Rheumatoid arthritis
 Sarcoidosis
 Sjogren syndrome
 Thrombosis
 Vitiligo

(preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands)

- IT 50-18-0, Cyclophosphamide 50-48-6, Amitriptyline 51-21-8,
 5-Fluorouracil 53-03-2, Prednisone 53-86-1, Indomethacin 57-22-7,
 Vincristine 59-05-2, Methotrexate 72-69-5, Nortriptyline
 298-46-4, Carbamazepine 378-44-9, β -Methasone 446-86-6,
 Azothioprine 599-79-1, Sulfasalazine 9005-49-6, Heparin, biological
 studies 15687-27-1, Ibuprofen 22071-15-4, Ketoprofen 22204-53-1,
 Naproxen 33069-62-4, Paclitaxel 36322-90-4, Piroxicam 60142-96-3,
 Gabapentin 65271-80-9, Mitoxantrone 75706-12-6, Leflunomide
 79217-60-0, Cyclosporin 84057-84-1, Lamotrigine 85622-93-1,
 Temozolomide 95058-81-4, Gemcitabine 105857-23-6, Alteplase
 143653-53-6, Abciximab 147245-92-9, Glatiramer acetate 148553-50-8,
 Pregabalin 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
 188627-80-7, Eftifibatide 191588-94-0, Tenecteplase
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (co-drug; preparation of isothiazole dioxides as CXC- and CC-chemokine
 receptor ligands)
- IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (co-drug; preparation of isothiazole dioxides as CXC- and CC-chemokine
 receptor ligands)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-

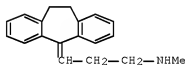
10/524815

dimethyl- (CA INDEX NAME)



RN 72-69-5 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 14 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:638859 ZCAPLUS Full-text

DOCUMENT NUMBER: 143:153384

TITLE: Preparation of diaminothiadiazoles as CXc- and CC-chemokine receptor ligands

INVENTOR(S): Biju, Purakkattil J.; Taveras, Arthur G.; Yu, Younong; Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.

PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.

SOURCE: PCT Int. Appl., 593 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066147	A1	20050721	WO 2004-US42060	20041216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

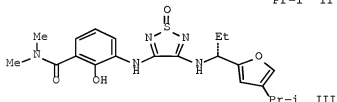
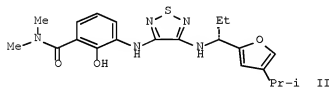
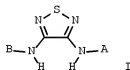
CA 2550189	A1	20050721	CA 2004-2550189	20041216
EP 1694659	A1	20060830	EP 2004-814266	20041216
EP 1694659	B1	20080827		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

US 20060223864	A1	20061005	US 2004-13753	20041216
US 7338968	B2	20080304		
CN 1918138	A	20070221	CN 2004-80041695	20041216
JP 2007514746	T	20070607	JP 2006-545364	20041216
AT 406356	T	20080915	AT 2004-814266	20041216
ES 2308299	T3	20081201	ES 2004-814266	20041216
MX 2006007076	A	20060831	MX 2006-7076	20060619
HK 1087711	A1	20081128	HK 2006-109781	20060904
US 20080090823	A1	20080417	US 2007-861870	20070926

PRIORITY APPLN. INFO.: US 2003-531311P P 20031219
US 2003-531713P P 20031222
US 2004-13753 A3 20041216
WO 2004-US42060 W 20041216

OTHER SOURCE(S): MARPAT 143:153384
GI



AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH₂), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepn. and/or

characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

IC ICM C07D285-10

ICS C07D417-12; C07D417-14; A61K031-433; A61K031-4436

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

IT AIDS (disease)

Acne

Alzheimer's disease

Analgesics

Anemia (disease)

Angiogenesis

Angiogenesis inhibitors

Anti-AIDS agents

Anti-Alzheimer's agents

Anti-ischemic agents

Antianginal agents

Antiarthritics

Antiasthmatics

Antidiabetic agents

Antimalarials

Antiphospholipid syndrome

Antirheumatic agents

Antitumor agents

Antitussives

Antiulcer agents

Antiviral agents

Arthritis

Asthma

Atherosclerosis

Behcet's syndrome

Burn

Celiac disease

Central nervous system, neoplasm

Cirrhosis

Combination chemotherapy

Common cold

Cough

Cystic fibrosis

Dermatomyositis

Diabetes mellitus

Drug delivery systems

Dyspnea

Emphysema

Encephalitis

Fibrosis

Gout

Graves' disease

Hepatitis virus

Herpesviridae

Human

Human herpesvirus

Human herpesvirus 8

Hypercapnia

Hypoxia

Immunomodulators

Lung, disease

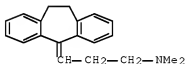
Lupus erythematosus

Malaria

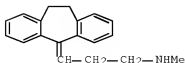
Meningitis
 Multiple organ failure
 Multiple sclerosis
 Myasthenia gravis
 Myelodysplastic syndromes
 Myositis
 Neoplasm
 Osteoarthritis
 Osteoporosis
 Pruritus
 Psoriasis
 Respiratory system, disease
 Rheumatoid arthritis
 Sarcoidosis
 Sjogren syndrome
 Thrombosis
 Vitiligo

(preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands)

- IT 50-48-6, Amitriptyline 53-86-1, Indomethacin 72-69-5
 , Nortriptyline 298-46-4, Carbamazepine 15687-27-1, Ibuprofen
 22071-15-4, Ketoprofen 22204-53-1, Naproxen 36322-90-4, Piroxicam
 60142-96-3, Gabapentin 84057-84-1, Lamotrigine 148553-50-8, Pregabalin
 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (co-drug; preparation of diaminothiadiazoles as CXC- and CC-chemokine
 receptor ligands)
- IT 50-48-6, Amitriptyline 72-69-5, Nortriptyline
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (co-drug; preparation of diaminothiadiazoles as CXC- and CC-chemokine
 receptor ligands)
- RN 50-48-6 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-
 dimethyl- (CA INDEX NAME)



- RN 72-69-5 ZCAPLUS
- CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-
 methyl- (CA INDEX NAME)



10/524815

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD
(2 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 15 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:99226 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:197859

TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,
9H-carbazole-4-carboxamides, and
dibenzo[b,d]thiophene-4-carboxamides as PDE4
inhibitors for the treatment of inflammatory and
allergic disorders

INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant A.;
Lakdawala, Aftab D.; Karunakaran, Usha

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals, Inc. USA, USA

SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of Appl.
No. PCT/IB04/000355.

CODEN: USXXCO

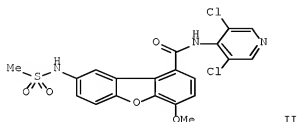
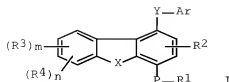
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050027129	A1	20050203	US 2004-821642	20040409
US 7223789	B2	20070529		
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411
WO 2004089940	A1	20041021	WO 2004-IB355	20040211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SN, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, BG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ZA 2005008240	A	20060531	ZA 2005-8240	20051012
US 20070105854	A1	20070510	US 2006-536434	20060928
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602
PRIORITY APPLN. INFO.:				
			IN 2003-MU363	A 20030411
			US 2003-519967P	P 20031113
			WO 2004-IB355	A2 20040211
			US 2004-821642	A3 20040409
			US 2006-536434	A1 20060928

OTHER SOURCE(S): MARPAT 142:197859
GI



- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6 (R5, R6 = H, alkyl, cycloalkyl, etc.), heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SOO-2, NRA; Y = CONR7, NR7SOO-2, SOO-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; Ra = H, alkyl, cycloalkyl, etc.; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1- carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D333-76
ICS C07D209-82; C07D307-91
- INCL 549048000; 548444000; 549460000
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;
tricyclic heterocycle prepn phosphodiesterase 4 inhibitor
antiinflammatory antiallergic antidiabetic
- IT Inflammation
(Crohn's disease, treatment of; preparation of tricyclic
heterocycles as PDE4 inhibitors for treatment of immune and
inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
(Crohn's, treatment of; preparation of tricyclic heterocycles as
PDE4 inhibitors for treatment of immune and inflammatory disorders and
insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treatment of; preparation of tricyclic
heterocycles as PDE4 inhibitors for treatment of immune and
inflammatory disorders and insulin resistant diabetes)

- IT Allergy
 - Inflammation
 - Nose, disease
 - (allergic rhinitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - (allergic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis
 - (atopic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease
 - (cerebrovascular, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease
 - Inflammation
 - (chronic bronchitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease
 - (chronic obstructive pulmonary disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - (chronic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (dementia, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (depression, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma
 - (eosinophilic, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease
 - (failure, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - (inflammation, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
 - Heart, disease
 - Intestine, disease
 - Joint, anatomical
 - Lung, disease
 - Skin, disease
 - (inflammatory conditions or immune disorders, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT Intestine, disease
 - (inflammatory, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus
 - (insulin-resistant, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - Kidney, disease
 - (nephritis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
 - Alzheimer's disease
 - Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Antiarthritics
 - Antiasthmatics
 - Antidepressants
 - Antidiabetic agents
 - Antirheumatic agents
 - Cardiovascular agents
 - Drug delivery systems
 - Human
 - Immunomodulators
 - Nervous system agents
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tricyclic compounds
 - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
 - Gout
 - Osteoarthritis
 - (rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - Spinal column, disease
 - (spondylitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - Amnesia
 - Asthma
 - Central nervous system, disease
 - Cystic fibrosis
 - Immune disease
 - Inflammation
 - Multiple sclerosis
 - Psoriasis
 - Respiratory distress syndrome
 - Rheumatoid arthritis
 - Shock (circulatory collapse)

Urticaria

(treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT Inflammation

Intestine, disease

(ulcerative colitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT Eye, disease

Inflammation

(uveitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(phenoxy carbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide
- RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-35-5P 778576-36-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(3-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

[bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-48-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isobutylloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 hydrochloride 778576-56-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-57-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[morpholin-4-
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[[1-
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-
 carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,
 N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-83-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-
 carboxamide 778576-87-7P 778576-88-8P 778576-89-9P,
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-hydroxy-2-
 oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-
 carboxamide 778576-95-7P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-96-8P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-97-9P,

N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-99-1P 778577-06-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778581-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 2973-58-2P, 2-Bromoisoavanillin 19688-46-1P,
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,
 4-Cyclopentyl-3-hydroxybenzaldehyde 685873-89-6P,
 2-Bromo-4-cyclopentyl-3-hydroxybenzaldehyde 685873-90-9P,
 2-Bromo-4-cyclopentyl-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,
 4-Cyclopentyl-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-carboxamide 778576-29-7P, Methyl 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P, 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P, N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 9036-21-9, Phosphodiesterase type 4
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 836627-26-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9, 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7, N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9, Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9, 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5, 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8, Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8, Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6, 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2004:1127375 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:74464

TITLE: Preparation of tricyclic compounds useful for the treatment of inflammatory and allergic disorders

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

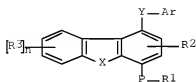
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

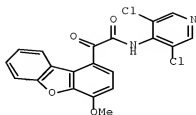
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111044	A1	20041223	WO 2004-1B1643	20040616
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

IN 2003MU00631	A	20050211	IN 2003-MU631	20030617
PRIORITY APPLN. INFO.:			IN 2003-MU631	A 20030617
OTHER SOURCE(S):	MARPAT 142:74464			
GI				



I



II

AB The title compds. I [R1-R3 = H, alkyl, cycloalkyl, aryl, etc.; n = 0-4; X = O, S(O)m, NRA (wherein m = 0-2; Ra = H, alkyl, cycloalkyl, etc.); P = O, S; Ar = (un)substituted aryl, arylalkyl, heterocyclyl, heteroaryl; Y = C(A)C(B)NR4 (wherein A, B = O, S, NRA; R4 = H, alkyl, OH, aryl, etc.)] which are novel phosphodiesterase type 4 (PDE4) inhibitors useful for the treatment of inflammatory and allergic disorders, were prepared Thus, reacting 2-(4-methoxydibenzo[b,f]furan-1-yl)-2-oxoacetic acid (preparation given) with 4-amino-3,5-dichloropyridine afforded II which showed IC50 of 184 nM against PDE4.

IC ICM C07D405-12

ICS A61K031-343

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

ST tricyclic compd prepn phosphodiesterase 4 PDE4 inhibitor

antiinflammatory; dibenzofuranyloxoacetamide prepn phosphodiesterase 4

PDE4 inhibitor antiinflammatory allergy asthma

IT Allergy inhibitors

Anti-Alzheimer's agents

Anti-inflammatory agents

Antiaesthetics

Antidepressants

Antidiabetic agents

Antirheumatic agents

Immunomodulators

(preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the treatment of inflammatory and allergic disorders)

IT Allergy

Alzheimer's disease

Amnesia

Asthma

Central nervous system, disease

Cystic fibrosis

Eczema

Gout

Immune disease

Inflammation

Multiple sclerosis

Osteoarthritis

Psoriasis

Rheumatoid arthritis

10/524815

Shock (circulatory collapse)

Urticaria

(treating; preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors

for

the treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 17 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:902155 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:384286

TITLE: Novel encochleation methods, cochleates and methods of
use

INVENTOR(S): Mannino, Raphael J.; Gould-Fogerite, Susan;
Krause-Elsmore, Sara L.; Delmarre, David; Lu, Ruying

PATENT ASSIGNEE(S): Biodelivery Sciences International, Inc., USA;
University of Medicine and Dentistry of New Jersey

SOURCE: PCT Int. Appl., 195 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091578	A2	20041028	WO 2004-US11026	20040409
WO 2004091578	A3	20050331		
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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 20050013854	A1	20050120	US 2004-822230	20040409
EP 1624858	A2	20060215	EP 2004-759375	20040409
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK			
US 20070237814	A1	20071011	US 2007-653434	20070111
US 20080009457	A1	20080110	US 2007-653093	20070111
PRIORITY APPLN. INFO.:			US 2003-461483P	P 20030409
			US 2003-463076P	P 20030415
			US 2003-499247P	P 20030828
			US 2003-502557P	P 20030911
			US 2003-532755P	P 20031224
			US 2004-537252P	P 20040115
			US 2004-556192P	P 20040324
			US 2004-822230	A1 20040409
			US 2004-822235	B1 20040409
			WO 2004-US11026	W 20040409
AB	The invention generally relates to cochleate drug delivery vehicles. Disclose are novel methods for making cochleates and cochleate compns. that include introducing a cargo moiety to a liposome in the presence of a solvent. Also			

disclosed are cochleates and cochleate comps. that include an aggregation inhibitor, and optionally, a cargo moiety. Addnl., anhydrous cochleates that include a protonized cargo moiety, a divalent metal cation and a neg. charge lipid are disclosed. Methods of using the cochleate comps. of the invention, including methods of administration, are also disclosed.

IC ICM A61K009-127

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 17, 18

IT Adenoma

Aggregation

Alopecia

Alzheimer's disease

Analgesics

Anesthetics

Animal virus

Anti-Alzheimer's agents

Anti-infective agents

Antiarthritics

Antiasthmatics

Antibacterial agents

Antibiotics

Anticholesteremic agents

Anticoagulants

Anticonvulsants

Antidepressants

Antidiabetic agents

Antihistamines

Antihypertensives

Antihypotensives

Antimicrobial agents

Antioesity agents

Antioxidants

Antiparkinsonian agents

Antipsychotics

Antirheumatic agents

Antitumor agents

Antiviral agents

Arthritis

Asthma

Atherosclerosis

Autoimmune disease

Biliary tract, neoplasm

Blood coagulation disorders

Carcinoma

Carcinoma

Cations

Chelating agents

Cholinergic antagonists

Cognition enhancers

Cystic fibrosis

Cytoprotective agents

Cytotoxic agents

Dairy products

Decongestants

Detergents

Eczema

Esophagus, neoplasm

Expectorants

Flavoring materials

Fungicides

Gene therapy
Genetic vectors
Ginkgo
Gout
Graves' disease
Gums and Mucilages
Headache
Hemophilia
Hemostatics
Hypercholesterolemia
Hyperglycemia
Hypericum
Hypertension
Hypolipemic agents
Hypotension
Imaging agents
Immune disease
Immunostimulants
Immunosuppressants
Infection
Inflammation
Leukemia
Leukotriene antagonists
Lung, neoplasm
Lymphoma
Malnutrition
Mammary gland, neoplasm
Melanoma
Milk
Mouthwashes
Multiple sclerosis
Muscular dystrophy
Myasthenia gravis
Mycosis
Neoplasm
Neuroglia, neoplasm
Nutrients
Obesity
Organelle
Osteoarthritis
Ovary, neoplasm
Packaging materials
Pain
Pancreas, neoplasm
Parasitocides
Parkinson's disease
Pigments, biological
Plasmids
Prostate gland, neoplasm
Psoriasis
Psychotropics
Rheumatoid arthritis
Sarcoma
Schizophrenia
Skin, disease
Stomach, neoplasm
Sweetening agents
Testis, neoplasm
Tranquilizers
Transplant rejection

Uterus, neoplasm

Vaccines

Vasoconstrictors

Vasodilators

Hyperlipidemia

RL: BIOL (Biological study)

(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

- IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies
 50-12-4, Mephenytoin 50-23-7, Hydrocortisone 50-24-8, Prednisolone
 50-48-6, Amitriptyline 50-49-7, Imipramine 51-61-6,
 Dopamine, biological studies 52-53-9, Verapamil 53-06-5, Cortisone
 53-86-1, Indomethacin 54-11-5, Nicotine 57-41-0, Phenytoin 57-92-1,
 Streptomycin, biological studies 58-22-0, Testosterone 58-82-2,
 Bradykinin 59-01-8, Kanamycin A 66-71-7, 1,10-Phenanthroline
 67-20-9, Nitrofurantoin 72-69-5, Nortriptyline 77-41-8,
 Methsuximide 77-67-8, Ethosuximide 79-09-4, Propionic acid, biological
 studies 86-34-0, Phensuximide 86-35-1, Ethotoin 89-57-6, Mesalamine
 103-90-2, Acetaminophen 110-91-8D, Morpholine, derivs. 112-38-9,
 Undecylenic acid 113-15-5D, Ergotamine, derivs. 113-53-1,
 Dothiepin 124-07-2, Caprylic acid, biological studies 125-33-7,
 Primidone 126-07-8, Griseofulvin 127-48-0, Trimethadione 128-46-1,
 Dihydrostreptomycin 130-26-7, Cloiquinol 148-82-3, Melphalan
 298-46-4, Carbamazepine 302-79-4, Vitamin A acid 303-49-1,
 Clomipramine 379-68-0, 18-Hydroxydeoxycorticosterone 439-14-5,
 Diazepam 458-37-7, Curcumin 512-64-1, Echinomycin 618-39-3,
 Benzamidine 645-05-6, Hexamethylmelamine 777-11-7, Haloprogin
 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamycin
 1404-04-2, Neomycin 1404-55-3, Ristocetin 1404-90-6, Vancomycin
 1421-14-3, Propanidid 1668-19-5, Doxepin 1695-77-8,
 Spectinomycin 2022-85-7, Flucytosine 2078-54-8, Propofol 2398-96-1,
 Tolnaftate 2809-21-4 3947-65-7, Neamine 4696-76-8, Kanamycin B
 7261-97-4, Dantrolene 7488-56-4, Selenium sulfide 7542-37-2,
 Paromomycin 7681-93-8, Natamycin 8067-82-1, Alphadione 9002-60-2,
 ACTH, biological studies 9004-10-8, Insulin, biological studies
 9007-12-9, Calcitonin 9034-40-6, LH-RH 9041-90-1, Angiotensin I
 9076-44-2, Chymostatin 11000-17-2, Vasopressin 11056-06-7, Bleomycin
 11128-99-7, Angiotensin II 12687-51-3, Angiotensin III 13292-46-1,
 Rifampin 14074-80-7, Zinc tetraphenyl porphyrin 15307-86-5, Diclofenac
 15687-27-1, Ibuprofen 19794-93-5, Trazodone 21829-25-4, Nifedipine
 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22832-87-7, Miconazole
 nitrate 22916-47-8, Miconazole 23047-25-8, Lofepiramine
 23593-75-1, Clotrimazole 24305-27-9, Thyroid releasing hormone
 25316-40-9, Adriamycin 25451-15-4, Felbamate 25546-65-0, Ribostamycin
 27220-47-9, Econazole 28721-07-5, Oxcarbazepine 29767-20-2, Teniposide
 30562-34-6, Geldanamycin 32986-56-4, Tobramycin 33069-62-4, Taxol
 33507-63-0, Substance P (peptide) 36322-90-4, Piroxicam 36357-77-4,
 Phosphoramidon 37321-09-8, Apramycin 37332-99-3, Avoparcin
 37517-28-5, Amikacin 37691-11-5, Antipain 39319-82-9, Actinoidin
 39324-30-6, Pepstatin 41621-49-2, Ciclopirox olamine 42924-53-8,
 Nabumetone 51050-59-0, 3,4-Dichloroisocoumarin 51110-01-1,
 Somatostatin 51798-45-9, Elastatinal 53123-88-9, Rapamycin
 54651-05-7, Echinocandin B 54910-89-3, Fluoxetine 55123-66-5,
 Leupeptin 56391-56-1, Netilmicin 58391-28-9, Leucokinin 58814-86-1,
 Aculeacin A 58970-76-6, Bestatin 59277-89-3, Acyclovir 59729-33-8,
 Citalopram 59865-13-3, Cyclosporin 60617-12-1, β -Endorphin
 61036-62-2, Teicoplanin 61318-90-9, Sulconazole 61869-08-7, Paroxetine
 64211-45-6, Oxiconazole 64872-76-0, Butoconazole 65277-42-1,
 Ketoconazole 65472-88-0, Naftifine 67655-94-1, Amastatin 67915-31-5,

Terconazole 68291-97-4, Zonisamide 70288-86-7, Ivermectin 71125-38-7, Meloxicam 71620-89-8, Reboxetine 74913-18-1, Dynorphin 78628-80-5, Terbinafine hydrochloride 79404-91-4, Cilofungin 79617-96-2, Sertraline 80619-41-6, Echinocandin 84057-84-1, Lamotrigine 84625-61-6, Itraconazole 85650-52-8, Mirtazapine 86386-73-4, Fluconazole 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 97240-79-4, Topiramate 101828-21-1, Butenafine 102767-28-2, Levetiracetam 105462-24-6 110588-57-3, Saperconazole 114977-98-2, Taxotere 118850-71-8 118850-72-9 118850-73-0 127779-20-8, Saquinavir 135882-23-4, Pneumocandin A4 137234-62-9, Voriconazole 150378-17-9, Indinavir 155213-67-5, Ritonavir 159445-62-2, Orientiparcin 159989-64-7, Nelfinavir 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 162808-62-0, Caspofungin 166663-25-8, Anidulafungin 235114-32-6, Micafungin
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

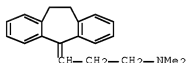
(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

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 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel encochleation methods and cochleates and methods of use for delivery of drugs and other agents using liposomes and aggregation inhibitors)

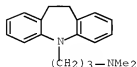
RN 50-48-6 ZCAPLUS

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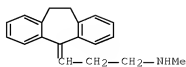
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CN 5H-Dibenz[b,f]azepine-5-propanamine, 10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)

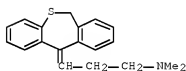


RN 72-69-5 ZCAPLUS

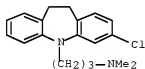
CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N-methyl- (CA INDEX NAME)



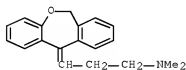
RN 113-53-1 ZCAPLUS
 CN 1-Propanamine, 3-dibenzo[b,e]thiepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



RN 303-49-1 ZCAPLUS
 CN 5H-Dibenz[b,f]azepine-5-propanamine, 3-chloro-10,11-dihydro-N,N-dimethyl- (CA INDEX NAME)



RN 1668-19-5 ZCAPLUS
 CN 1-Propanamine, 3-dibenz[b,e]oxepin-11(6H)-ylidene-N,N-dimethyl- (CA INDEX NAME)



RN 23047-25-8 ZCAPLUS
 CN Ethanone, 1-(4-chlorophenyl)-2-[[3-(10,11-dihydro-5H-dibenz[b,f]azepin-5-yl)propyl]methylamino]- (CA INDEX NAME)

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
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 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2003M000363 A 20050304 IN 2003-MU363 20030411
 AU 2004228453 A1 20041021 AU 2004-228453 20040211
 CA 2522023 A1 20041021 CA 2004-2522023 20040211
 EP 1620429 A1 20060201 EP 2004-710093 20040211
 EP 1620429 B1 20090401

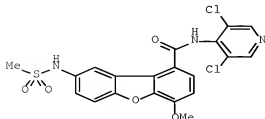
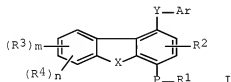
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 JP 2006522789 T 20061005 JP 2006-506259 20040211
 NZ 542882 A 20071026 NZ 2004-542882 20040211
 AT 427308 T 20090415 AT 2004-710093 20040211
 ES 2320888 T3 20090529 ES 2004-710093 20040211
 AP 2008 A 20090630 AP 2005-3424 20040211
 US 20050027129 A1 20050203 US 2004-821642 20040409
 US 7223789 B2 20070529
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 NO 2005005316 A 20060111 NO 2005-5316 20051110
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 US 7384962 B2 20080610
 US 20070105855 A1 20070510 US 2006-536448 20060928
 US 7393846 B2 20080701
 US 20090182143 A1 20090716 US 2008-131286 20080602

PRIORITY APPLN. INFO.:

IN 2003-MU363 A 20030411
 US 2003-519967P P 20031113
 WO 2004-IB355 W 20040211
 US 2004-821642 A3 20040409
 US 2006-536434 A1 20060928

OTHER SOURCE(S): CASREACT 141:366121; MARPAT 141:366121
 GI



- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6, heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRa; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1- carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D405-12
ICS C07D405-14; C07D307-91; C07D401-12; C07D409-12; A61K031-4427; A61P029-00
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic; tricyclic heterocycle prepn phosphodiesterase 4 inhibitor antiinflammatory antiallergic antidiabetic
- IT Inflammation
(Crohn's disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
(Crohn's, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Inflammation
Nose, disease
(allergic rhinitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
(allergic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis
(atopic, rheumatoid, treatment of; preparation of tricyclic

- heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease
 - (cerebrovascular, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease
 - Inflammation
 - (chronic bronchitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease
 - (chronic obstructive pulmonary disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - (chronic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Anti-inflammatory agents
 - (chronic; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (dementia, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (depression, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma
 - (eosinophilic, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease
 - (failure, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - (inflammation, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
- Heart, disease
- Intestine, disease
- Joint, anatomical
- Lung, disease
- Skin, disease
 - (inflammatory conditions or immune disorders, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
 - (inflammatory, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus
 - (insulin-resistant, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT Inflammation
 - Kidney, disease
 - (nephritis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
 - Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Antiarthritics
 - Antiasthmatics
 - Antidepressants
 - Antidiabetic agents
 - Antirheumatic agents
 - Cardiovascular agents
 - Drug delivery systems
 - Human
 - Immunomodulators
 - Nervous system agents
 - Polymorphism (crystal)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tumor necrosis factors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tricyclic compounds
 - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
 - Gout
 - Osteoarthritis
 - (rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - Spinal column, disease
 - (spondylitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - Amnesia
 - Asthma
 - Central nervous system, disease
 - Cystic fibrosis
 - Immune disease
 - Inflammation
 - Multiple sclerosis
 - Psoriasis
 - Respiratory distress syndrome
 - Rheumatoid arthritis
 - Shock (circulatory collapse)
 - Urticaria
 - (treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and

- insulin resistant diabetes)
- IT Inflammation
- Intestine, disease
- (ulcerative colitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[2-ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide
- RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
- (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-35-5P 778576-36-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[3-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-bis[(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

[[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 hydrochloride 778576-56-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-57-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[morpholin-4-
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[1-
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-
 carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P,
 N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-83-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-
 carboxamide 778576-87-7P 778576-88-8P 778576-89-9P,
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[1-(2-hydroxy-2-
 oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-
 carboxamide 778576-95-7P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-
 methyl-6-[(methylsulfonyl)amino]-9H-carbazole-4-carboxamide
 778576-96-8P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-
 [(ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-
 carbazole-4-carboxamide 778576-98-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt
 778576-99-1P 778577-06-3P, N-(3,5-Dichloropyridin-4-yl)-4-
 difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[fur-2-
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778581-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 2973-58-2P, 2-Bromoisoavanillin 19688-46-1P,
3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,
3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,
2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,
4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,
4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,
4-Cyclopentylloxy-3-hydroxybenzaldehyde 685873-89-6P,
2-Bromo-4-cyclopentylloxy-3-hydroxybenzaldehyde 685873-90-9P,
2-Bromo-4-cyclopentylloxy-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,
4-Cyclopentylloxy-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,
4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,
4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,
4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,
N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,
N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,
N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-carboxamide 778576-29-7P, Methyl 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P, 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P, N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P 778577-04-1P 778577-05-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

- IT 9036-21-9, Phosphodiesterase type 4 9040-59-9, Phosphodiesterase 1 9068-52-4, Phosphodiesterase type 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9, 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7, N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9, Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9, 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5,

2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isonitrillin 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8, Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8, Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6, 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7, 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl 3-amino-4-methoxybenzoate 778576-75-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ACCESSION NUMBER: 2004:675744 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:207059

TITLE: Tricyclic compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

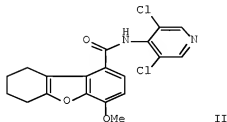
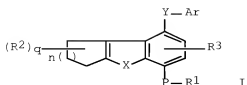
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069831	A1	20040819	WO 2004-IB330	20040210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00177	A	20050204	IN 2003-MU177	20030210
PRIORITY APPLN. INFO.:			IN 2003-MU177	A 20030210
OTHER SOURCE(S):	MARPAT	141:207059		
GI				



- AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocycl(yl)(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocycl(yl)(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaiacol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.
- IC ICM C07D405-12
ICS C07D409-12; C07D401-12; C07D307-92; A61K031-343; A61K031-381; A61K031-403
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- ST tricyclic prepn phosphodiesterase 4 inhibitor antiinflammatory
antiallergic; pyridyl dibenzofuran dibenzothiophene carbazole PDE4
inhibitor inflammation allergy treatment
- IT Allergy inhibitors
Anti-Alzheimer's agents
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antidiabetic agents
Cardiovascular agents

Cognition enhancers
 Immunomodulators
 Immunosuppressants
 Nervous system agents
 (preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

IT Alzheimer's disease
 Amnesia
 Asthma
 Central nervous system, disease
 Cystic fibrosis
 Eczema
 Gout
 Immune disease
 Inflammation
 Multiple sclerosis
 Osteoarthritis
 Psoriasis
 Respiratory distress syndrome
 Rheumatoid arthritis
 Shock (circulatory collapse)
 Urticaria
 (treatment of; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 20 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:370918 ZCAPLUS Full-text

DOCUMENT NUMBER: 140:391192

TITLE: Preparation of dibenzofuran/dibenzothiophene derivatives useful for the treatment of inflammatory and allergic disorders

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 254 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037805	A1	20040506	WO 2003-IB4442	20031008
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

IN 2002MU00922	A	20050304	IN 2002-MU922	20021023
CA 2503015	A1	20040506	CA 2003-2503015	20031008
AU 2003269317	A1	20040513	AU 2003-269317	20031008
EP 1554262	A1	20050720	EP 2003-751096	20031008
EP 1554262	B1	20071205		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

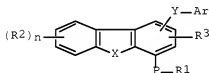
BR 2003014721	A	20050802	BR 2003-14721	20031008
CN 1729181	A	20060201	CN 2003-80107246	20031008
JP 2006506379	T	20060223	JP 2004-546246	20031008
AT 380185	T	20071215	AT 2003-751096	20031008
ES 2298552	T3	20080516	ES 2003-751096	20031008
ZA 2005002969	A	20060222	ZA 2005-2969	20050413
US 20060178418	A1	20060810	US 2005-532273	20050926
US 7238725	B2	20070703		
US 20080146810	A1	20080619	US 2007-769074	20070627

PRIORITY APPLN. INFO.:

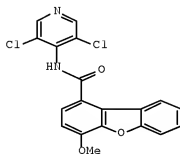
IN 2002-MU922	A	20021023
WO 2003-IB4442	W	20031008
US 2005-532273	A1	20050926

OTHER SOURCE(S): MARPAT 140:391192

GI



I



II

AB Title compds. I [R1-3 = H, alk(en/yn)yl, cycloalkyl, etc.; P = O, S; n = 0-4; Ar = (un)substituted aryl, etc.; Y = carboxamido, aminosulfonyl, etc.] are prepared For instance, 4-methoxydibenzofuran-1-carboxylic acid (preparation given) is converted to the corresponding acid chloride (PhH, SOCl₂, reflux, 4 h) and treated with 4-amino-3,5-dichloropyridine (DMF/THF, NaH, -10°) to give II. II has IC₅₀ = 0.8 nM for PDE4. I are useful for the treatment of inflammatory conditions, diseases of the central nervous and insulin resistant diabetes.

IC ICM C07D307-91
ICS C07D333-76; C07D209-88; C07D405-12; C07D401-12; C07D409-12; C07D405-14; A61K031-403; A61K031-34; A61K031-381; A61P037-00; A61P025-00; A61P003-10

CC 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST tricyclic dibenzofuran dibenzothiophene inflammatory allergic process
prepn

IT Alzheimer's disease
Amnesia
Anti-inflammatory agents

Antiarthritics
 Antiasthmatics
 Antidepressants
 Antidiabetic agents
 Antirheumatic agents
 Asthma
 Cystic fibrosis
 Diabetes insipidus
 Diabetes mellitus
 Gout
 Human
 Immune disease
 Inflammation
 Multiple sclerosis
 Nervous system agents
 Osteoarthritis
 Psoriasis
 Respiratory distress syndrome
 Rheumatoid arthritis

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

OS.CITING REF COUNT: 11 THERE ARE 11 CAPLUS RECORDS THAT CITE THIS
 RECORD (12 CITINGS)
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 21 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:935594 ZCAPLUS Full-text

DOCUMENT NUMBER: 136:69730

TITLE: Preparation of

1,3-bis-(substituted-phenyl)-2-propen-1-ones as VCAM-1
 inhibitors for treatment of inflammatory disorders
 Meng, Charles Q.; Ni, Liming; Sikorski, James A.;
 Hoong, Lee K.

PATENT ASSIGNEE(S): Atherogenics, Inc., USA

SOURCE: PCT Int. Appl., 220 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

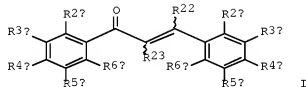
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098291	A2	20011227	WO 2001-US19720	20010620
WO 2001098291	A3	20020516		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2413878	A1	20011227	CA 2001-2413878	20010620
BR 2001011889	A	20030624	BR 2001-11889	20010620
EP 1330448	A2	20030730	EP 2001-946583	20010620
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

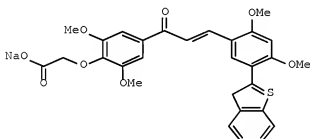
US 6608101	B1	20030819	US 2001-886348	20010620
JP 2004501147	T	20040115	JP 2002-504247	20010620
NZ 523443	A	20041126	NZ 2001-523443	20010620
MX 2002012660	A	20040514	MX 2002-12660	20021218
IN 2003DN00008	A	20060609	IN 2003-DN8	20030101
ZA 2003000134	A	20051006	ZA 2003-134	20030106
US 20030236298	A1	20031225	US 2003-443470	20030521
US 7078431	B2	20060718		
ZA 2005003708	A	20070425	ZA 2005-3708	20050509
US 20060258735	A1	20061116	US 2006-485940	20060713
PRIORITY APPLN. INFO.:			US 2000-212769P	P 20000620
			US 2000-255934P	P 20001215
			US 2001-886348	A1 20010620
			WO 2001-US19720	W 20010620
			US 2003-443470	A1 20030521

OTHER SOURCE(S): MARPAT 136:69730

GI



I



II

AB Title compds. I [wherein R2a, R3a, R4a, R5a, R6a, R2b, R3b, R4b, R5b, and R6b = independently H, (cyclo)alkyl, (hetero)aryl, carbocyclyl, (halo)alkylthio, (un)substituted alkoxy or amino, (halo)acyl, amido, (halo)alkylsulfonyl, aminocarbonyl, alkenyl, alkynyl, halo, OH, SH, CN, NO₂, SO₃H, sulf(on)amido, PO₃H₂, alditol, carbohydrate, amino acid, etc.; R22 and R23 = independently H or alkyl; or R22 and R6a or R23 and R6a can join together to form a bridged carbocycle, (hetero)aryl, or heterocycle; R2a and R3a, R3a and R4a, R4a and R5a, R5a and R6a, R2b and R3b, R3b and R4b, R4b and R5b, or R5b and R6b and independently join to form a bridged (un)substituted carbocycle, cycloalkenyl, cycloalk(en)ylcarbonyl, (hetero)aryl, heterocycle, or alkylenedioxy; and the E or Z isomers thereof] were prepared to inhibit the expression of VCAM-1. For example, 3',5'-dimethoxy-4'-hydroxyacetophenone was treated with Et glycolate, PPh₃, and di-Et azodicarboxylate in THF to give 4'-ethoxycarbonylmethoxy-3',5'-dimethoxyacetophenone (90%). Coupling the acetophenone and 5-(benzo[b]thien-2-yl)-2,4-dimethoxybenzaldehyde (preparation given) in the presence of NaOH in absolute EtOH afforded the 1,3-diphenyl-2-propen-1-one II (39%), which stimulated cultured human aortic smooth muscle cell activity with

IC50 of 0.45 μ M. I are useful for the treatment of inflammatory disorders that are mediated by VCAM-1, including arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

IC ICM C07D333-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Cystic fibrosis

Dermatitis

Graves' disease

Psoriasis

Transplant rejection

(treatment; preparation of bis(substituted phenyl)propenones as VCAM-1 inhibitors for treatment of inflammatory disorders)

IT Antidepressants

(tricyclic; co-administration of bis(substituted phenyl)propenone VCAM-1 inhibitors with other biol. agents)

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 22 OF 49 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:338762 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to

a pharmaceutical agent from gene expression profile

Farr, Spencer

INVENTOR(S): Phase-1 Molecular Toxicology, USA

PATENT ASSIGNEE(S): PCT Int. Appl., 222 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a

subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IC ICM C12Q001-68

ICS G01N033-50

CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 1, 6, 7, 13, 15

IT CFTR (cystic fibrosis transmembrane conductance regulator)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(methods of determining individual hypersensitivity to a pharmaceutical

agent

from gene expression profile)

IT 50-02-2, Dexamethasone 50-06-6, Phenobarbital, biological studies
 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8,
 Prednisolone 50-28-2, Estradiol, biological studies 50-44-2,
 6-Thiopurine 50-48-6, Amitriptyline 50-55-5, Reserpine
 50-76-0, Actinomycin D 50-78-2, Aspirin 51-06-9, Procainamide
 51-21-8, Fluorouracil 51-34-3, Scopolamine 51-48-9, Levothyroxine,
 biological studies 51-49-0, Dextrothyroxine 51-55-8, Atropine,
 biological studies 51-75-2, Mechlorethamine 52-01-7, Spironolactone
 52-53-9, Verapamil 52-67-5, Penicillamine 52-86-8, Haloperidol
 53-03-2, Prednisone 53-06-5, Cortisone 53-19-0, Mitotane 53-33-8,
 Paramethasone 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5,
 Nicotine 54-31-9, Furosemide 54-36-4, Metyrapone 54-85-3, Isoniazid
 55-63-0, Nitroglycerin 55-65-2, Guanethidine 55-98-1, Busulfan
 56-54-2, Quinidine 56-75-7, Chloramphenicol 57-22-7, Vincristine
 57-41-0, Phenytoin 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol
 57-66-9, Probenecid 57-83-0, Progesterone, biological studies 57-96-5,
 Sulfipyrazole 58-05-9, Leucovorin 58-14-0, Pyrimethamine 58-32-2,
 Dipyradomole 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9,
 Theophylline, biological studies 58-61-7, Adenosine, biological studies
 58-74-2, Papaverine 58-93-5, Hydrochlorothiazide 58-94-6, Thiazide
 59-05-2, Methotrexate 59-42-7, Phenylephrine 59-43-8, Thiamine,
 biological studies 59-92-7, Levodopa, biological studies 59-99-4,
 Neostigmine 60-40-2, Mecamylamine 60-54-8, Tetracycline 60-79-7,
 Ergonovine 60-87-7, Promethazine 61-32-5, Methicillin 61-72-3,
 Cloxacillin 64-75-5, Tetracycline hydrochloride 64-77-7, Tolbutamide
 64-86-8, Colchicine 65-23-6, Pyridoxine 66-79-5, Oxacillin 66-97-7,
 Psoralen 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-68-5,
 Dimethyl sulfoxide, biological studies 68-22-4D, Norethindrone, mixture
 with ethinyl estradiol 68-41-7, Cycloserine 68-88-2, Hydroxyzine
 69-53-4, Ampicillin 69-72-7, biological studies 69-89-6, Xanthine
 73-24-5, 6-Aminopurine, biological studies 73-31-4, Melatonin 76-42-6,
 Oxycodone 76-57-3, Codeine 77-09-8, Phenolphthalein 77-19-0,
 Dicyclomine 77-36-1, Chlorthalidone 78-44-4, Carisoprodol 80-08-0,
 Dapsone 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 82-92-8,
 Cyclizine 82-95-1, Buclizine 83-43-2, Methylprednisolone 83-73-8,

Iodoquinol 83-89-6, Quinacrine 83-98-7, Orphenadrine 86-54-4,
 Hydralazine 89-57-6, Mesalamine 90-34-6, Primaquine 90-82-4,
 Pseudoephedrine 91-64-5, Coumarin 92-13-7, Pilocarpine 92-84-2,
 Phenothiazine 93-14-1, Guaifenesin 94-20-2, Chlorpropamide 94-36-0,
 Benzoyl peroxide, biological studies 94-78-0, Phenazopyridine 95-25-0,
 Chlorzoxazone 96-64-0, Soman 97-77-8, Disulfiram 99-66-1, Valproic
 acid 100-33-4, Pentamidine 100-97-0, Methenamine, biological studies
 101-31-5, Hyoscycamine 103-90-2, Acetaminophen 113-18-8, Ethchlorvynol
 113-42-8, Methylergonovine 113-45-1, Methylphenidate 114-07-8,
 Erythromycin 114-86-3, Phenformin 118-42-3, Hydroxychloroquine
 122-09-8, Phentermine 123-56-8, Succinimide 123-63-7, Paraldehyde
 124-94-7, Triamcinolone 125-29-1, Hydrocodone 125-33-7, Primidone
 125-64-4, Methylpyrrolone 125-71-3, Dextromethorphan 125-84-8,
 Aminoglutethimide 126-07-8, Griseofulvin 126-52-3, Ethinamate
 127-07-1, Hydroxyurea 127-69-5, Sulfisoxazole 128-13-2, Ursodiol
 130-95-0, Quinine 132-17-2, Benztropine 133-10-8, Sodium
 p-aminosalicylate 137-58-6, Lidocaine 138-56-7, Trimethobenzamide
 144-11-6, Trihexyphenidyl 147-52-4, Nafcillin 147-94-4, AraC
 148-82-3, Melphalan 154-21-2, Lincomycin 154-42-7, Thioguanine
 154-93-8, Carmustine 155-97-5, Pyridostigmine 298-46-4,
 5H-Dibenz[b,f]azepine-5-carboxamide 298-50-0, Propantheline 299-42-3,
 Ephedrine 300-62-9D, Amphetamine, mixed 300-62-9D, Amphetamine, mixed
 salts 302-17-0, Chloral hydrate 302-79-4, Tretinoin 303-53-7,
 Cyclobenzaprine 305-03-3, Chlorambucil 315-30-0, Allopurinol
 321-64-2, Tacrine 346-18-9, Polythiazide 361-37-5, Methylsergide
 363-24-6, Dinoprostone 364-62-5, Metoclopramide 378-44-9,
 Betamethasone 389-08-2, Nalidixic acid 395-28-8, Isoxsuprine
 439-14-5, Diazepam 443-48-1, Metronidazole 446-86-6, Azathioprine
 456-59-7, Cyclandelate 461-72-3, Hydantoin 463-04-7, Amyl nitrite
 469-62-5, Propoxyphene 474-25-9, Chenodiol 480-30-8,
 Dichlorophenazone 484-23-1, Dihydralazine 503-01-5, Isometheptene
 512-15-2, Cyclopentolate 520-85-4, Medroxyprogesterone 525-66-6,
 Propanolol 526-36-3, Xylometazoline 536-33-4, Ethionamide 541-15-1,
 Levocarnitine 546-88-3, Acetohydroxamic acid 555-30-6, Methyl dopa
 564-25-0, Doxycycline 569-65-3, Meclizine 577-11-7, Docusate sodium
 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 603-50-9, Bisacodyl
 634-03-7, Phendimetrazine 637-07-0, Clofibrate 657-24-9, Metformin
 671-16-9, Procarbazine 672-87-7, Metyrosine 674-38-4, Bethanechol
 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 745-65-3,
 Alprostadil 791-35-5, Chlophedianol 797-63-7, Levonorgestrel
 797-64-8D, L-Norgestrel, ethinyl estradiol mixture 846-49-1, Lorazepam
 846-50-4, Temazepam 911-45-5, Clomiphene 915-30-0, Diphenoxylate
 962-58-3, Diazoxon 968-93-4, Testolactone 972-02-1, Diphenidol
 990-73-8, Fentanyl citrate 1134-47-0, Baclofen 1143-38-0, Anthralin
 1321-13-7, Potassium aminobenzoate 1397-89-3, Amphotericin B
 1400-61-9, Nystatin 1404-04-2, Neomycin 1404-04-2D, Neomycin, mixture
 with polymyx/HC 1404-90-6, Vancomycin 1406-05-9, Penicillin
 1491-59-4, Oxymetazoline 1622-61-3, Clonazepam 1953-02-2, Tiopronin
 1977-10-2, Loxapine 2152-34-3, Pemoline 2152-44-5, Betamethasone
 valerate 2447-57-6, Sulfadoxine 2451-01-6, Terpin hydrate 2609-46-3,
 Amiloride 2809-21-4 2998-57-4, Estramustine 3116-76-5, Dicloxacillin
 3313-26-6, Thiothixene 3385-03-3, Flunisolide 3485-14-1, Cyclacillin
 3737-09-5, Disopyramide
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (methods of determining individual hypersensitivity to a pharmaceutical
 agent from gene expression profile)

IT 3778-73-2, Iphoshamide 3930-20-9, Sotalol 4205-90-7, Clonidine
 4419-39-0, Beclomethasone 4499-40-5, Oxtriphylline, biological studies

4618-18-2, Lactulose 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin
 5051-62-7, Guanabenz 5543-57-7, (s)-Warfarin 5633-20-5, Oxycodone
 5786-21-0, Clozapine 6190-39-2, Dihydroergotamine mesylate 6493-05-6,
 Pentoxifylline 6621-47-2, Perhexiline 7020-55-5, Clidinium
 7235-40-7, Beta carotene 7261-97-4, Danrolene 7416-34-4, Molindone
 7439-93-2, Lithium, biological studies 7447-40-7, Potassium chloride,
 biological studies 7481-89-2, Zalcitabine 7487-88-9, Magnesium
 sulfate, biological studies 7648-98-8, Ambenonium 7681-11-0, Potassium
 iodide, biological studies 7681-93-8, Natamycin 7683-59-2,
 Isoproterenol 8029-99-0, Paregoric 8049-47-6, Pancreatin 8050-81-5,
 Simethicone 8063-07-8, Kanamycin 8067-24-1, Ergoloid mesylates
 9001-27-8, BLOOD-coagulation factor VIII 9001-75-6, Pepsin 9004-10-8,
 Insulin, biological studies 9004-67-5, Methyl cellulose 9005-49-6,
 Enoxaparin, biological studies 9007-92-5, Glucagon, biological studies
 9039-53-6, Urokinase 9046-56-4, Ancrod 10118-90-8, Minocycline
 10238-21-8, Glyburide 10262-69-8, Maprotiline 10540-29-1,
 Tamoxifen 11041-12-6, Cholestyramine 11056-06-7, Bleomycin
 11111-12-9, Cephalosporin 12174-11-7, Attapulgit 12244-57-4, Gold
 sodium thiomalate 12650-69-0, Mupirocin 12794-10-4b, Benzodiazepine,
 derivs. 13010-47-4, Lomustine 13292-46-1, Rifampin 13311-84-7,
 Flutamide 13392-28-4, Rimantadine 13647-35-3, Trilostane
 14028-44-5, Amoxapine 14124-50-6 14611-51-9, Selegiline
 14769-73-4, Levamisole 14838-15-4, Phenylpropanolamine 14882-18-9,
 Bismuth subsalicylate 15301-69-6, Flavoxate 15307-86-5, Diclofenac
 15663-27-1, Cisplatin 15686-71-2, Cephalaxin 15687-27-1, Ibuprofen
 15722-48-2, Olsalazine 16051-77-7, Isosorbide mononitrate 16068-46-5,
 Potassium phosphate 16110-51-3, Cromolyn 16590-41-3, Naltrexone
 16679-58-6, Desmopressin 17230-88-5, Danazol 17784-12-2, Sulfacytine
 18323-44-9, Clindamycin 18559-94-9, Albuterol 18883-66-4, Streptozocin
 19216-56-9, Prazosin 19794-93-5, Trazodone 20537-88-6, Amifostine
 20830-75-5, Digoxin 20830-81-3, Daunomycin 21256-18-8, Oxaprozin
 21829-25-4, Nifedipine 22204-53-1, Naproxen 22232-71-9, Mazindol
 23031-32-5, Terbutaline sulfate 23214-92-8, Doxorubicin 23288-49-5,
 Probucol 25322-68-3, Polyethylene glycol 25451-15-4, Felbamate
 25614-03-3, Bromocriptine 25812-30-0, Gemfibrozil 26652-09-5,
 Ritodrine 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8,
 Timolol 27203-92-5, Tramadol 27262-47-1, Levobupivacaine 27686-84-6,
 Masoprocil 28395-03-1, Bumetanide 28657-80-9, Cinoxacin 28782-42-5,
 Difenoxin 28860-95-9, Carbidozole 28911-01-5, Triazolam 28981-97-7,
 Alprazolam 29094-61-9, Glipizide 29110-47-2, Guanfacine 29122-68-7,
 Atenolol 30516-87-1, Zidovudine 31441-78-8, Mercaptopurine
 31677-93-7, Bupropion hydrochloride 31828-71-4, Mexiletine 31883-05-3,
 Moricizine 32986-56-4, Tobramycin 33069-62-4, Pacitaxel 33419-42-0,
 Etoposide 34089-81-1, Sodium ferric gluconate 35189-28-7, Norgestimate
 36322-90-4, Piroxicam 36505-84-7, Buspirone 36791-04-5, Ribavirin
 38304-91-5, Minoxidil 40180-04-9, Tienilic acid 40580-59-4, Guanadrel
 41575-94-4, Carboplatin 41708-72-9, Tocainide 42399-41-7, Diltiazem
 42924-53-8, Nabumetone 49562-28-9, Fenofibrate 50679-08-8, Terfenadine
 50925-79-6, Colestipol 50972-17-3, Bacampicillin 51022-71-0, Nabilone
 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol
 51481-61-9, Cimetidine 53179-11-6, Loperamide 53230-10-7, Mefloquine
 53608-75-6, Pancrelipase 53714-56-0, Leuprolide 53994-73-3, Cefaclor
 54024-22-5, Desogestrel 54063-53-5, Propafenone 54143-56-5, Flcainide
 acetate 54182-58-0, Sucralfate 54350-48-0, Etretinate 54573-75-0,
 Doxercalciferol 54910-89-3, Fluoxetine 55142-85-3, Ticlopidine
 55268-75-2, Cefuroxime 55985-32-5, Nicardipine 56420-45-2, Epirubicin
 58001-44-8 58581-89-8, Azelastine 59122-46-2, Misoprostol
 59277-89-3, Acyclovir 59729-33-8, Citalopram 59865-13-3, Cyclosporine
 A 60142-96-3, Gabapentin 60205-81-4, Ipratropium 61489-71-2,
 Menotropin 61718-82-9, Fluvoxamine maleate 61869-08-7, Paroxetine

62571-86-2, Captopril 63585-09-1, Foscarnet sodium 63590-64-7,
 Terazosin 64952-97-2, Latamoxef 65141-46-0, Nicorandil 65277-42-1,
 Ketoconazole 66085-59-4, Nimodipine 66104-22-1, Pergolide
 66357-35-5, Ranitidine 66376-36-1, Alendronate 67227-57-0, Fenoldopam
 mesylate 68475-42-3, Anagrelide 68844-77-9, Astemizole 69049-73-6,
 Nedocromil 69123-98-4, Fialuridine 69655-05-6, Didanosine
 70359-46-5, Brominide tartrate 70989-04-7, S-Mephenytoin 71320-77-9,
 Moclobemide 72432-03-2, Miglitol 72509-76-3, Felodipine 72956-09-3,
 Carvedilol 73590-58-6, Omeprazole 74103-06-3, Ketorolac 74191-85-8,
 Doxazosin 75330-75-5, Lovastatin 75695-93-1, Isradipine 75706-12-6,
 Leflunomide 75847-73-3, Enalapril 76470-66-1, Loracarbef 76547-98-3,
 Lisinopril 76568-02-0, Flosequin 76584-70-8 76824-35-6, Famotidine
 76932-56-4, Nafarelin 76963-41-2, Nizatidine 78110-38-0, Aztreonam
 78628-80-5, Terbinafine hydrochloride 79516-68-0, Levocabastine
 79617-96-2, Sertraline 79794-75-5, Loratadine 79902-63-9, Simvastatin
 80125-14-0, Remoxipride 80474-14-2, Fluticasone propionate 81093-37-0,
 Pravastatin 81098-60-4, Cisapride 81103-11-9, Clarithromycin
 81669-57-0, Anistreplase 82410-32-0, Ganciclovir 82419-36-1, Ofloxacin
 82626-48-0, Zolpidem 82834-16-0, Perindopril 83366-66-9, Nefazodone
 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5,
 Azithromycin 84057-84-1, Lamotrigine 84449-90-1, Raloxifene
 84625-61-6, Itraconazole 85441-61-8, Quinapril 85721-33-1,
 Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril
 87333-19-5, Ramipril 87679-37-6, Trandolapril 88040-23-7, Cefepime
 88150-42-9, Amlodipine 89365-50-4, Salmeterol 89778-26-7, Toremifene
 90566-53-3, Fluticasone 91714-94-2, Bromfenac
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical

agent

from gene expression profile)

IT 50-48-6, Amitriptyline 10262-69-8, Maprotiline

14028-44-5, Amoxapine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)

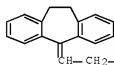
(methods of determining individual hypersensitivity to a pharmaceutical

agent

from gene expression profile)

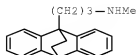
RN 50-48-6 ZCAPLUS

CN 1-Propanamine, 3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)-N,N-
 dimethyl- (CA INDEX NAME)

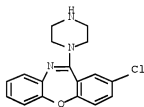


RN 10262-69-8 ZCAPLUS

CN 9,10-Ethanoanthracene-9(10H)-propanamine, N-methyl- (CA INDEX NAME)



RN 14028-44-5 ZCAPLUS
 CN Dibenz[b,f][1,4]oxazepine, 2-chloro-11-(1-piperazinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD
 (5 CITINGS)
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 23 OF 49 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 2003571445 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 14605211
 TITLE: Human targets of *Pseudomonas aeruginosa* pyocyanin.
 AUTHOR: Ran Huimin; Hassett Daniel J; Lau Gee W
 CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine,
 University of Cincinnati College of Medicine, 231 Albert
 Sabin Way, Cincinnati, OH 45267-0564, USA.
 SOURCE: Proceedings of the National Academy of Sciences of the
 United States of America, (2003 Nov 25) Vol. 100, No. 24,
 pp. 14315-20. Electronic Publication: 2003-11-06.
 Journal code: 7505876. ISSN: 0027-8424.
 Report No.: NLM-PMC283589.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (IN VITRO)
 Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200402
 ENTRY DATE: Entered STN: 16 Dec 2003
 Last Updated on STN: 3 Feb 2004
 Entered Medline: 2 Feb 2004

ABSTRACT:
Pseudomonas aeruginosa produces copious amounts of the redoxactive tricyclic
 compound pyocyanin that kills competing microbes and mammalian cells,
 especially during cystic fibrosis lung infection. Cross-phylum
 susceptibility to pyocyanin suggests the existence of evolutionarily conserved

physiological targets. We screened a *Saccharomyces cerevisiae* deletion library to identify presumptive pyocyanin targets with the expectation that similar targets would be conserved in humans. Fifty *S. cerevisiae* targets were provisionally identified, of which 60% have orthologous human counterparts. These targets encompassed major cellular pathways involved in the cell cycle, electron transport and respiration, epidermal cell growth, protein sorting, vesicle transport, and the vacuolar ATPase. Using cultured human lung epithelial cells, we showed that pyocyanin-mediated reactive oxygen intermediates inactivate human vacuolar ATPase, supporting the validity of the yeast screen. We discuss how the inactivation of V-ATPase may negatively impact the lung function of cystic fibrosis patients.

CONTROLLED TERM: Apoptosis: DE, drug effects
 Cell Line
 Drug Resistance, Fungal
 Electron Transport: DE, drug effects
 Genes, Bacterial
 Genes, Fungal: DE, drug effects
 Humans
 Oxidative Stress: DE, drug effects
 *Pseudomonas aeruginosa: PY, pathogenicity
 *Pyocyanine: TO, toxicity
 Saccharomyces cerevisiae: DE, drug effects
 Saccharomyces cerevisiae: GE, genetics
 Saccharomyces cerevisiae: ME, metabolism
 Sequence Deletion
 Vacuolar Proton-Translocating ATPases: GE, genetics
 Vacuolar Proton-Translocating ATPases: ME, metabolism

CAS REGISTRY NO.: 85-66-5 (Pyocyanine)
 CHEMICAL NAME: EC 3.6.1.- (Vacuolar Proton-Translocating ATPases)

L91 ANSWER 24 OF 49 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2003474605 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 14550580
 TITLE: Benefits of different drug formulations in psychopharmacology.
 AUTHOR: Frijlink Henderik W
 CORPORATE SOURCE: Department of Pharmaceutical Technology and Biopharmacy, Groningen University Institute for Drug Exploration, Groningen, The Netherlands.. frijlink@farm.rug.nl
 SOURCE: European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology, (2003 Sep) Vol. 13 Suppl 3, pp. S77-84. Ref: 24
 Journal code: 9111390. ISSN: 0924-977X.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200311
 ENTRY DATE: Entered STN: 11 Oct 2003
 Last Updated on STN: 19 Dec 2003
 Entered Medline: 21 Nov 2003

ABSTRACT:

Adequate dosage forms are essential for achieving successful pharmacotherapy. Innovative dosage forms or delivery systems may direct a drug to its specific site of action, optimize the timing of the drug release, or increase comfort or convenience for the patient. Thus, such innovations may improve efficacy and tolerability and lead to improvements in health-related quality of life. Specialized dosage forms (e.g., depot injections, extended-release formulations) of several psychiatric agents have been extensively used. The

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latest addition is an orally disintegrating formulation of the antidepressant mirtazapine. This dosage form dissolves rapidly in the mouth and is convenient for the large proportion of patients who have difficulty in swallowing tablets.

CONTROLLED TERM: Anti-Bacterial Agents: AD, administration & dosage
*Chemistry, Pharmaceutical
Circadian Rhythm
Cystic Fibrosis: DT, drug therapy
Drug Administration Routes
*Drug Delivery Systems
Humans
Mianserin: AD, administration & dosage
*Mianserin: AA, analogs & derivatives
Mianserin: ME, metabolism
Patient Compliance
Proton Pumps: AD, administration & dosage
Proton Pumps: AI, antagonists & inhibitors
*Psychopharmacology

CAS REGISTRY NO.: 24219-97-4 (Mianserin); 61337-67-5 (mirtazapine)
CHEMICAL NAME: 0 (Anti-Bacterial Agents); 0 (Proton Pumps)

L91 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 1993192191 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8448110
TITLE: Sequence-selective binding of amiloride to DNA.
AUTHOR: Bailly C; Cuthbert A W; Gentle D; Knowles M R; Waring M J
CORPORATE SOURCE: Department of Pharmacology, University of Cambridge, U.K.
SOURCE: Biochemistry, (1993 Mar 16) Vol. 32, No. 10, pp. 2514-24.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 23 Apr 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 13 Apr 1993

ABSTRACT:

Nuclease footprinting techniques have been employed to investigate the interaction between the diuretic drug amiloride, a sodium channel blocker with potential therapeutic use in the treatment of cystic fibrosis, and three DNA fragments of defined sequence. Using either DNase I or micrococcal nuclease as probes, an unusual pattern of sequence-selective recognition of DNA has been detected. Amiloride binds selectively to sites rich in adenine and thymine residues, frequently with an apparent preference for 5'-TpX-3' steps, and discriminates strongly against GC-rich sequences which are sometimes cut more readily in the presence of the drug compared to the control. A detailed comparison with the actions of known selective DNA-binding antibiotics and drugs reveals a unique pattern of binding sites, different from those of typical intercalators on the one hand and those of minor groove-binders on the other. Amiloride is believed to adopt a pH-dependent tricyclic hydrogen-bonded conformation in solution which allows it to intercalate into DNA; consistent with this belief, we find that the footprinting pattern largely disappears at pH values above the pKa. Preliminary studies with three amiloride analogues have indicated the importance of two functional groups in the recognition of DNA. The possible relevance of selective DNA binding to activity in vivo is considered.

CONTROLLED TERM: *Amiloride: CH, chemistry

Base Sequence
 Binding Sites
 *DNA: CH, chemistry
 *DNA, Bacterial: CH, chemistry
 Deoxyribonuclease I
 Escherichia coli: GE, genetics
 *Intercalating Agents
 Kinetics
 Molecular Sequence Data
 *Oligodeoxyribonucleotides: CH, chemistry
 Plasmids
 Promoter Regions, Genetic
 RNA, Transfer, Tyr: GE, genetics
 2609-46-3 (Amiloride); 9007-49-2 (DNA)
 CAS REGISTRY NO.: 0 (DNA, Bacterial); 0 (Intercalating Agents); 0
 CHEMICAL NAME: 0 (Oligodeoxyribonucleotides); 0 (RNA, Transfer, Tyr); 0
 (T-DNA); EC 3.1.21.1 (Deoxyribonuclease I)
 GENE NAME: tyr

L91 ANSWER 26 OF 49 MEDLINE on STN
 ACCESSION NUMBER: 2004554886 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 15526520
 TITLE: Pulmonary involvement in diabetes mellitus.
 AUTHOR: Nicolaie I; Zavoianu Cristina; Nuta P
 CORPORATE SOURCE: 2nd Clinic of Internal Medicine, Central Emergency Clinic
 Military Hospital, Bucharest, Romania..
 nicolaiee8@yahoo.com
 SOURCE: Romanian journal of internal medicine = Revue roumaine de
 medecine interne, {2003} Vol. 41, No. 4, pp. 365-74.
 Ref: 44
 Journal code: 9304507. ISSN: 1220-4749.
 PUB. COUNTRY: Romania
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200411
 ENTRY DATE: Entered STN: 6 Nov 2004
 Last Updated on STN: 20 Dec 2004
 Entered Medline: 30 Nov 2004

ABSTRACT:
 Diabetes mellitus involves the lungs in the course of the complex phenomena it generates. Recent research in animal diabetes as well as in human diabetes demonstrated biochemical changes at the pulmonary level such as the suppression of aniline p-hydroxylase, the reduction of the activity of glutathione-peroxidase, the development of NO-dependent endothelial dysfunction, microsomal disorders, increased heparan sulphate at the level of the vascular basement membrane, increased levels of advanced glycation end-products and the derangement of bronchial mucus production by amyline. Structural modifications of the lung parenchyma were observed such as the narrowing of the alveolar space, the flattening of the alveolar epithelium and the expansion of the interstitium. Aside from the involvement of the pulmonary vessels there is the involvement of the basement membranes of the alveolar epithelium, the bronchial epithelium and the pulmonary capillaries. The consequences of local oxidative stress, the increased vascular permeability and the modifications in mucus secretion lead to the reduction of pulmonary volumes, pulmonary diffusion capacity, elastic recoil with involvement of restrictive lung disorders, diminished bronchial reactivity and diminished bronchodilatation. Data of pulmonary pathology obtained from patients as well as pulmonary involvement of children born of diabetic mothers are presented

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succinctly.

CONTROLLED TERM: Animals
 Basement Membrane: PA, pathology
 Cystic Fibrosis: CO, complications
 Diabetes Complications
 *Diabetes Mellitus: PA, pathology
 *Diabetes Mellitus: PP, physiopathology
 Endothelium, Vascular: PA, pathology
 Glycosylation End Products, Advanced: ME, metabolism
 Humans
 *Lung: PA, pathology
 Lung Diseases: PA, pathology
 Lung Diseases: PP, physiopathology
 Pulmonary Alveoli: PA, pathology
 Pulmonary Alveoli: PP, physiopathology
 Respiratory Tract Infections: PA, pathology
 Respiratory Tract Infections: PP, physiopathology
CHEMICAL NAME: 0 (Glycosylation End Products, Advanced)

L91 ANSWER 27 OF 49 MEDLINE on STN
ACCESSION NUMBER: 1983307213 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6764592
TITLE: [Iatrogenic pathology of the optic nerve].
 Pathologie iatrogene du nerf optique.
AUTHOR: Hamard H; Desbordes J M
SOURCE: L'Annee therapeutique et clinique en ophtalmologie,
 {1982} Vol. 33, pp. 185-202. Ref: 27
 Journal code: 0405351. ISSN: 0301-4495.
 Report No.: PIP-019579; POP-00131382.
PUB. COUNTRY: France
DOCUMENT TYPE: (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
LANGUAGE: French
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 198310
ENTRY DATE: Entered STN: 19 Mar 1990
 Last Updated on STN: 1 Nov 2002
 Entered Medline: 8 Oct 1983

ABSTRACT:

Iatrogenic pathology of the optic nerve is examined according to a framework which distinguishes direct and indirect effects on the optic nerve. Direct effects due to toxic drugs should be suspected when unexplained, usually bilateral loss of visual acuity occurs. The 3 clinical stages of classical optic toxic neuropathy are 1) anomalies of color vision, 2) loss of visual acuity and narrowing field of vision, and 3) papillary palor corresponding to irreversible optic atrophy. Usually only the 1st stages are reversible, but the reversibility may be incomplete. The list of drugs which can cause such effects is lengthy and includes antiinfectious drugs such as sulfamides and derivatives of hydroxyquinoleins, chloramphenicol especially when used to treat cystic fibrosis of the pancreas in children, the antituberculins ethambutol in high doses and isoniazide, which occasion particular risks when combined; antiparasitics such as quinine and its derivatives chloroquine and hydroxychloroquine, which cause optic neuropathy through their effect on the retina; arsenic pentavalents such as tryparsamide, quinacrine, trecator and mystatin; drugs affecting the central nervous system such as monoamineoxidase inhibitors, laroxyyl, phenothiazine and the barbituates; anticonvulsants such as phenytoin; antimitotics such as vincristine; digitalics, disulfiram; penicillamines, and pexid. The action of lasers on the optic nerve can have a similar effect. The optic nerve may be indirectly damaged during surgical

procedures leading to hypotonia, acute ischemia of the head of the optic nerve or embolic accident after a local or regional injection. Damage may also be caused by radiotherapy of intracranial tumors and certain drugs which cause isolated papillary edema or edema associated with headaches, such as Tetracycline, large doses of vitamin A or D, corticoids, and oral contraceptive (OC) pills, which may cause papillary edema through cerebral pseudo-tumors that regress with discontinuation of treatment. This condition has been observed in women with uncontrolled hyperlipidemia. It is probable that an alteration of axonal transport is at the basis of the neuropathic mechanisms. The 1st step in therapy is the suppression of the toxin, or at least its discontinuation. Some success has been obtained with vitamin B therapy, corticotherapy, zinc, or isaxoxine, depending on the specific condition.

SUPPLEMENTARY TERM: Biology; Central Nervous System Effects; Contraception; Contraceptive Agents; Contraceptive Agents, Female; Contraceptive Methods--side effects; Drugs; Family Planning; Headache; Lipid Metabolic Effects; Ophthalmological Effects; Oral Contraceptives--side effects; Physiology; Reproductive Control Agents; Treatment
Check Tags: Female

CONTROLLED TERM: Adrenal Cortex Hormones: AE, adverse effects
Antiprotozoal Agents: AE, adverse effects
Chloramphenicol: AE, adverse effects
Contraceptives, Oral: AE, adverse effects
Ethambutol: AE, adverse effects
Humans
Iatrogenic Disease
Isoniazid: AE, adverse effects
Monoamine Oxidase Inhibitors: AE, adverse effects
*Optic Nerve Diseases: ET, etiology
Optic Nerve Diseases: TH, therapy
Phenytoin: AE, adverse effects
Quinine: AA, analogs & derivatives
Radiotherapy: AE, adverse effects
Surgical Procedures, Operative: AE, adverse effects
Vitamins: AE, adverse effects

CAS REGISTRY NO.: 130-95-0 (Quinine); 54-85-3 (Isoniazid); 56-75-7 (Chloramphenicol); 57-41-0 (Phenytoin); 74-55-5 (Ethambutol)

CHEMICAL NAME: 0 (Adrenal Cortex Hormones); 0 (Antiprotozoal Agents); 0 (Contraceptives, Oral); 0 (Monoamine Oxidase Inhibitors); 0 (Vitamins)

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ACCESSION NUMBER: 2003500456 EMBASE Full-text
TITLE: Human targets of *Pseudomonas aeruginosa* pyocyanin.
AUTHOR: Ran, Huimin; Lau, Gee W. (correspondence)
CORPORATE SOURCE: Div. of Pulmon./Critical Care Med., Univ. of Cincinnati Coll. of Med., 231 Albert Sabin Way, Cincinnati, OH 45267-0564, United States. gee.lau@uc.edu
AUTHOR: Hassett, Daniel J.
CORPORATE SOURCE: Department of Molecular Genetics, Univ. of Cincinnati Coll. of Med., 231 Albert Sabin Way, Cincinnati, OH 45267-0564, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (25 Nov 2003) Vol. 100, No. SUPPL. 2, pp. 14315-14320.
Refs: 63
ISSN: 0027-8424 CODEN: PNASAG
COUNTRY: United States

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DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2004
Last Updated on STN: 5 Jan 2004

ABSTRACT: *Pseudomonas aeruginosa* produces copious amounts of the redoxactive tricyclic compound pyocyanin that kills competing microbes and mammalian cells, especially during cystic fibrosis lung infection. Cross-phylum susceptibility to pyocyanin suggests the existence of evolutionarily conserved physiological targets. We screened a *Saccharomyces cerevisiae* deletion library to identify presumptive pyocyanin targets with the expectation that similar targets would be conserved in humans. Fifty *S. cerevisiae* targets were provisionally identified, of which 60% have orthologous human counterparts. These targets encompassed major cellular pathways involved in the cell cycle, electron transport and respiration, epidermal cell growth, protein sorting, vesicle transport, and the vacuolar ATPase. Using cultured human lung epithelial cells, we showed that pyocyanin-mediated reactive oxygen intermediates inactivate human vacuolar ATPase, supporting the validity of the yeast screen. We discuss how the inactivation of V-ATPase may negatively impact the lung function of cystic fibrosis patients.

CONTROLLED TERM: Medical Descriptors:
animal cell
article
calcium homeostasis
cell killing
cystic fibrosis
DNA library
electron transport
gene deletion
genetic susceptibility
hospital infection
lung function
microbial growth
nonhuman
oxidation reduction reaction
priority journal
**Pseudomonas aeruginosa*
Saccharomyces cerevisiae
*target cell
CONTROLLED TERM: Drug Descriptors:
*pyocyanine
CAS REGISTRY NO.: (pyocyanine) 85-66-5

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ACCESSION NUMBER: 2003351713 EMBASE Full-text
TITLE: Ciprofloxacin-induced renal insufficiency in cystic fibrosis.
AUTHOR: Moffett, Brady S.
CORPORATE SOURCE: Department of Pharmacy, Johns Hopkins Medical Institutions, 600 N. Wolfe Street, Park 316, Baltimore, MD 21287, United States.
AUTHOR: Rosenstein, Beryl J.; Mogayzel Jr., Peter J.
(correspondence)
CORPORATE SOURCE: Eudowood Div. Pediatric Resp. Sci., Johns Hopkins Medical Institutions, 600 N. Wolfe Street, Park 316, Baltimore, MD 21287, United States. mogayzel@mail.jhmi.edu

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AUTHOR: Moffett, Brady S.
CORPORATE SOURCE: Texas Children's Hospital, Department of Pharmacy, 6621 Fannin Street, Houston, TX 77030, United States.
SOURCE: Journal of Cystic Fibrosis, (Sep 2003) Vol. 2, No. 3, pp. 152-154.
Refs: 15
ISSN: 1569-1993 CODEN: JCFOAC
PUBLISHER IDENT.: S 1569-1993(03)00059-6
COUNTRY: Netherlands
DOCUMENT TYPE: Journal, Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Sep 2003
Last Updated on STN: 11 Sep 2003
ABSTRACT: Acute renal insufficiency is known to occur in patients who are taking ciprofloxacin, particularly the elderly. We report two young patients with cystic fibrosis who presented with acute renal insufficiency after 2-3 weeks of oral ciprofloxacin therapy. The incidence of this adverse effect in children and young adults who have cystic fibrosis is unknown. Multiple mechanisms for ciprofloxacin-induced nephrotoxicity have been proposed.
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CONTROLLED TERM: Medical Descriptors:
*acute kidney failure: SI, side effect
adolescent
adult
anorexia: SI, side effect
article
case report
*cystic fibrosis
drug induced disease: SI, side effect
echography
elderly care
female
human
incidence
laboratory test
lung infection: DT, drug therapy
Mycobacterium intracellulare avium
nausea: SI, side effect
nephrotoxicity: SI, side effect
Pseudomonas aeruginosa
Stenotrophomonas maltophilia
symptomatology
urinalysis
vomiting: SI, side effect
CONTROLLED TERM: Drug Descriptors:
aminoglycoside antibiotic agent: DT, drug therapy
aminoglycoside antibiotic agent: IV, intravenous drug administration
azithromycin: DT, drug therapy
*ciprofloxacin: AE, adverse drug reaction

*ciprofloxacin: CB, drug combination
 *ciprofloxacin: DT, drug therapy
 *ciprofloxacin: PO, oral drug administration
 clarithromycin: CB, drug combination
 clarithromycin: DT, drug therapy
 cotrimoxazole: DT, drug therapy
 dornase alfa: DT, drug therapy
 ethambutol: AE, adverse drug reaction
 ethambutol: CB, drug combination
 ethambutol: DT, drug therapy
 fluticasone propionate plus salmeterol
 isoniazid: AE, adverse drug reaction
 isoniazid: CB, drug combination
 isoniazid: DT, drug therapy
 nortriptyline
 omeprazole: DT, drug therapy
 pancreas enzyme: DT, drug therapy
 pyridoxine: CB, drug combination
 pyridoxine: DT, drug therapy
 rifabutin: AE, adverse drug reaction
 rifabutin: CB, drug combination
 rifabutin: DT, drug therapy
 salbutamol
 theophylline
 tobramycin: DT, drug therapy
 tobramycin: IH, inhalational drug administration
 vitamin

CAS REGISTRY NO.: (azithromycin) 83905-01-5; (ciprofloxacin) 85721-33-1;
 (clarithromycin) 81103-11-9; (cotrimoxazole) 8064-90-2;
 (dornase alfa) 143831-71-4; (ethambutol) 10054-05-4,
 1070-11-7, 3577-94-4, 74-55-5; (isoniazid) 54-85-3,
 62229-51-0, 65979-32-0; (nortriptyline) 72-69-5,
 894-71-3; (omeprazole) 73590-58-6, 95510-70-6; (pyridoxine)
 12001-77-3, 58-56-0, 65-23-6, 8059-24-3; (rifabutin)
 72559-06-9; (salbutamol) 18559-94-9; (theophylline)
 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9;
 (tobramycin) 32986-56-4

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ACCESSION NUMBER: 2003396282 EMBASE Full-text
 TITLE: Benefits of different drug formulations in psychopharmacology.
 AUTHOR: Frijlink, Henderik W. (correspondence)
 CORPORATE SOURCE: Dept. Pharmaceutical Technol./B., Groningen Univ. Inst. Drug Explor., Groningen, Netherlands. frijlink@farm.rug.nl
 SOURCE: European Neuropsychopharmacology, (Sep 2003) Vol. 13, No. SUPPL. 3, pp. S77-S84.
 Refs: 24
 ISSN: 0924-977X CODEN: EURNES
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
 FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 032 Psychiatry
 037 Drug Literature Index
 039 Pharmacy
 006 Internal Medicine
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 16 Oct 2003

Last Updated on STN: 16 Oct 2003

ABSTRACT: Adequate dosage forms are essential for achieving successful pharmacotherapy. Innovative dosage forms or delivery systems may direct a drug to its specific site of action, optimize the timing of the drug release, or increase comfort or convenience for the patient. Thus, such innovations may improve efficacy and tolerability and lead to improvements in health-related quality of life. Specialized dosage forms (e.g., depot injections, extended-release formulations) of several psychiatric agents have been extensively used. The latest addition is an orally disintegrating formulation of the antidepressant mirtazapine. This dosage form dissolves rapidly in the mouth and is convenient for the large proportion of patients who have difficulty in swallowing tablets. .COPYRGT. 2003 Elsevier B.V./ECNP. All rights reserved.

CONTROLLED TERM: Medical Descriptors:
 allergy
 asthma
 bioequivalence
 cancer
 chronic obstructive lung disease
 chronotherapy
 circadian rhythm
 circadian rhythm sleep disorder
 conference paper
 congestive heart failure
 cystic fibrosis: DT, drug therapy
 cystic fibrosis: EP, epidemiology
 cystic fibrosis: PC, prevention
 diabetes mellitus: DT, drug therapy
 drug absorption
 drug delivery system
 drug dosage form
 *drug formulation
 drug release
 epilepsy
 glaucoma
 human
 Human immunodeficiency virus infection
 hyperlipidemia
 hypertension: DT, drug therapy
 immunosuppressive treatment
 infection prevention
 inhaler
 kidney transplantation
 medical nebulizer
 mental disease: DT, drug therapy
 nebulization
 patient compliance
 peptic ulcer
 postmenopause
 priority journal
 *psychopharmacology
 quality of life
 rheumatoid arthritis
 tuberculosis

CONTROLLED TERM: Drug Descriptors:
 amfebutamone: DT, drug therapy
 amfebutamone: PR, pharmaceuticals
 antibiotic agent: DT, drug therapy
 antibiotic agent: IH, inhalational drug administration

antibiotic agent: PR, pharmaceuticals
 antidepressant agent: DT, drug therapy
 antidepressant agent: PO, oral drug administration
 antidepressant agent: PR, pharmaceuticals
 antidepressant agent: PK, pharmacokinetics
 calcium channel blocking agent: DT, drug therapy
 calcium channel blocking agent: PR, pharmaceuticals
 colistin: DT, drug therapy
 colistin: IH, inhalational drug administration
 colistin: PR, pharmaceuticals
 ethinylestradiol plus etonogestrel: PR, pharmaceuticals
 etonogestrel: PR, pharmaceuticals
 flupentixol: DT, drug therapy
 flupentixol: PR, pharmaceuticals
 fluphenazine: DT, drug therapy
 fluphenazine: PR, pharmaceuticals
 gestagen: PR, pharmaceuticals
 haloperidol: DT, drug therapy
 haloperidol: PR, pharmaceuticals
 immunosuppressive agent
 insulin: DT, drug therapy
 insulin: IH, inhalational drug administration
 insulin: PR, pharmaceuticals
 insulin: SC, subcutaneous drug administration
 levonorgestrel: PR, pharmaceuticals
 mirtazapine: DT, drug therapy
 mirtazapine: PO, oral drug administration
 mirtazapine: PR, pharmaceuticals
 mirtazapine: PK, pharmacokinetics
 mirtazapine soltab
 omeprazole: PO, oral drug administration
 omeprazole: PR, pharmaceuticals
 proton pump inhibitor: PO, oral drug administration
 proton pump inhibitor: PR, pharmaceuticals
 serotonin uptake inhibitor: DT, drug therapy
 serotonin uptake inhibitor: PR, pharmaceuticals
 tobramycin: DT, drug therapy
 tobramycin: IH, inhalational drug administration
 tobramycin: PR, pharmaceuticals
 venlafaxine: DT, drug therapy
 venlafaxine: PO, oral drug administration
 venlafaxine: PR, pharmaceuticals
 verapamil: DT, drug therapy
 verapamil: PR, pharmaceuticals

CAS REGISTRY NO.: (amfebutamone) 31677-93-7, 34911-55-2; (colistin)
 1066-17-7, 1264-72-8; (etonogestrel) 54048-10-1;
 (flupentixol) 2413-38-9, 2709-56-0; (fluphenazine)
 146-56-5, 69-23-8; (haloperidol) 52-86-8; (insulin)
 9004-10-8; (levonorgestrel) 797-63-7; (mirtazapine)
 61337-67-5; (omeprazole) 73590-58-6, 95510-70-6;
 (tobramycin) 32986-56-4; (venlafaxine) 93413-69-5;
 (verapamil) 152-11-4, 52-53-9

CHEMICAL NAME: (1) implanon; (2) mirena; (3) nuvaring; implanon; mirena
 COMPANY NAME: (1) Organon; (2) Schering; (3) Organon

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ACCESSION NUMBER: 2002335727 EMBASE Full-text

TITLE: Rofecoxib-induced instant aquagenic wrinkling of the palms.

AUTHOR: Carder, K. Robin; Weston, William L., Dr. (correspondence)

10/524815

CORPORATE SOURCE: Department of Dermatology, Univ. of CO Health Sciences
Center, Box B-153, 4200 E. 9th Ave., Denver, CO 80262,
United States. william.weston@uchsc.edu

SOURCE: Pediatric Dermatology, (Jul 2002) Vol. 19, No. 4, pp.
353-355.

Refs: 12

ISSN: 0736-8046 CODEN: PEDRDQ

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 013 Dermatology and Venereology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 10 Oct 2002

Last Updated on STN: 10 Oct 2002

ABSTRACT: An 18-year-old woman presented with a 3-week complaint of exaggerated palmar wrinkling and swelling following brief exposure (1-2 minutes) of her hands to water. She had a history of mixed connective tissue disease and had been started on rofecoxib therapy 1 month prior to the onset of her skin symptoms. Discontinuation of rofecoxib was followed by resolution of symptoms within a period of 3 weeks. Similar palmar skin changes following water exposure have been reported to occur in cystic fibrosis and are thought to be due to increased salt content of the skin and secondary increased water-binding capacity. Rofecoxib is a selective COX-2 inhibitor that has been shown to increase sodium reabsorption in the kidney via effects on prostaglandin E2 and the renal vasculature. The COX-2 protein is also expressed in keratinocytes and plays a role in keratinocyte differentiation. Prostaglandin E2 also plays a role in keratinocyte proliferation and differentiation. Thus rofecoxib may cause increased sodium reabsorption in the skin, as it does in the kidney. The rofecoxib-associated elevation in skin sodium may increase keratin water-binding capacity and cause exaggerated aquagenic wrinkling of the skin, as occurs in cystic fibrosis.

CONTROLLED TERM: Medical Descriptors:
adult
article
case report
cell differentiation
cell proliferation
connective tissue disease: DT, drug therapy
cystic fibrosis
differential diagnosis
drug mechanism
drug withdrawal
female
human
hydrophilicity
keratinocyte
*palmar dermatoglyphics
priority journal
protein expression
*skin manifestation: SI, side effect
sodium absorption
water immersion

CONTROLLED TERM: Drug Descriptors:
amitriptyline
loratadine
methotrexate: DT, drug therapy

methotrexate: IM, intramuscular drug administration
 naproxen
 nifedipine
 pantoprazole
 ranitidine

*rofecoxib: AE, adverse drug reaction

*rofecoxib: DT, drug therapy

*rofecoxib: PD, pharmacology

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (loratadine) 79794-75-5; (methotrexate) 15475-56-6, 59-05-2, 7413-34-5; (naproxen) 22204-53-1, 26159-34-2; (nifedipine) 21829-25-4; (pantoprazole) 102625-70-7; (ranitidine) 66357-35-5, 66357-59-3; (rofecoxib) 162011-90-7, 186912-82-3

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ACCESSION NUMBER: 2001380111 EMBASE Full-text

TITLE: Antioxidants: An integrative approach.

AUTHOR: Lachance, Paul A., Dr. (correspondence); Nakat, Zeina; Jeong, Woo-Sik

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science, Rutgers, State University of New Jersey, New Brunswick, NJ, United States. lachance@aesop.rutgers.edu

AUTHOR: Lachance, Paul A., Dr. (correspondence)

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science, Rutgers, State University of New Jersey, 65 Dudley Road, New Brunswick, NJ 08901-8520, United States. lachance@aesop.rutgers.edu

AUTHOR: Lachance, Paul A., Dr. (correspondence)

CORPORATE SOURCE: Nutraceuticals Institute, Department of Food Science, State University of New Jersey, 65 Dudley Road, New Brunswick, NJ 08901-8520, United States. lachance@aesop.rutgers.edu

SOURCE: Nutrition, (2001) Vol. 17, No. 10, pp. 835-838.

Refs: 46

ISSN: 0899-9007 CODEN: NUTRER

PUBLISHER IDENT.: S 0899-9007(01)00636-0

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 016 Cancer
 029 Clinical and Experimental Biochemistry
 046 Environmental Health and Pollution Control

LANGUAGE: English

ENTRY DATE: Entered STN: 15 Nov 2001

Last Updated on STN: 15 Nov 2001

CONTROLLED TERM: Medical Descriptors:
 adult respiratory distress syndrome
 aging
 *antioxidant activity
 asthma
 cancer
 cardiovascular disease
 cell function
 chronic bronchitis
 chronic obstructive lung disease
 cigarette smoking
 cystic fibrosis
 diet supplementation
 electron transport
 emphysema

human
immunity
lipid peroxidation
lung fibrosis
mineral dust
*oxidative stress
physical stress
pneumonia
priority journal
review

CONTROLLED TERM:

Drug Descriptors:
*alpha tocopherol
amine oxidase (flavin containing): EC, endogenous compound
amitriptyline
asbestos
ascorbic acid
beta carotene
catalase: EC, endogenous compound
ciprofloxacin
cyclosporin A
cytochrome c oxidase: EC, endogenous compound
*free radical
glutathione
glutathione peroxidase: EC, endogenous compound
hydrogen peroxide
imipramine
nitric oxide
nitrogen dioxide
oxygen radical
ozone
paracetamol
polychlorinated biphenyl
reactive oxygen metabolite
scavenger
superoxide dismutase: EC, endogenous compound
tamoxifen

CAS REGISTRY NO.:

xanthine oxidase: EC, endogenous compound
(alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4,
58-95-7, 59-02-9; (amine oxidase (flavin containing))
37255-42-8, 9001-66-5, 9059-11-4; (amitriptyline)
50-48-6, 549-18-8; (asbestos) 1332-21-4; (ascorbic
acid) 134-03-2, 15421-15-5, 50-81-7; (beta carotene)
7235-40-7; (catalase) 9001-05-2; (ciprofloxacin)
85721-33-1; (cyclosporin A) 59865-13-3, 63798-73-2;
(cytochrome c oxidase) 72841-18-0, 9001-16-5; (glutathione
peroxidase) 9013-66-5; (glutathione) 70-18-8; (hydrogen
peroxide) 7722-84-1; (imipramine) 113-52-0, 50-49-7;
(nitric oxide) 10102-43-9; (nitrogen dioxide) 10102-44-0;
(ozone) 10028-15-6; (paracetamol) 103-90-2; (superoxide
dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (tamoxifen)
10540-29-1; (xanthine oxidase) 9002-17-9

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ACCESSION NUMBER: 2000090698 EMBASE Full-text

TITLE: PharmaCE test questions.

SOURCE: Annals of Pharmacotherapy, (2000) Vol. 34, No. 3, pp. 413.
ISSN: 1060-0280 CODEN: APHRER

COUNTRY: United States

DOCUMENT TYPE: Journal; Note

10/524815

FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery

LANGUAGE: English

ENTRY DATE: Entered STN: 23 Mar 2000
Last Updated on STN: 23 Mar 2000

CONTROLLED TERM: Medical Descriptors:
*antibiotic therapy
clinical feature
cystic fibrosis
drug contraindication
drug disposition
drug indication
drug induced disease: ET, etiology
drug induced disease: SI, side effect
drug research
external otitis: DT, drug therapy
group therapy
human
nightmare: DT, drug therapy
note
otitis media: DT, drug therapy
*posttraumatic stress disorder: DI, diagnosis
*posttraumatic stress disorder: DT, drug therapy
*posttraumatic stress disorder: TH, therapy
priority journal
*psychopharmacotherapy
rating scale
salmonellosis: DT, drug therapy

CONTROLLED TERM: Drug Descriptors:
amfebutamone: DT, drug therapy
amitriptyline: DT, drug therapy
*antidepressant agent: DT, drug therapy
buspirone: DT, drug therapy
ciprofloxacin: AE, adverse drug reaction
ciprofloxacin: DT, drug therapy
ciprofloxacin: PK, pharmacokinetics
clonazepam: DT, drug therapy
clozapine: DT, drug therapy
cyproheptadine: DT, drug therapy
desipramine: DT, drug therapy
fluoxetine: DT, drug therapy
fluvoxamine: DT, drug therapy
guanfacine: DT, drug therapy
imipramine: DT, drug therapy
lithium: DT, drug therapy
nefazodone: DT, drug therapy
ofloxacin: AE, adverse drug reaction
ofloxacin: DT, drug therapy
ofloxacin: PK, pharmacokinetics
paroxetine: DT, drug therapy
pefloxacin: AE, adverse drug reaction
pefloxacin: DT, drug therapy
pefloxacin: PK, pharmacokinetics
propranolol: DT, drug therapy
*quinoline derived antiinfective agent: AE, adverse drug reaction
*quinoline derived antiinfective agent: DT, drug therapy
*quinoline derived antiinfective agent: PK,

pharmacokinetics
 risperidone: DT, drug therapy
 valproic acid: DT, drug therapy
 (amfebutamone) 31677-93-7, 34911-55-2; (amitriptyline)
 50-48-6, 549-18-8; (buspirone) 33386-08-2, 36505-84-7;
 (ciprofloxacin) 85721-33-1; (clonazepam) 1622-61-3;
 (clozapine) 5786-21-0; (cyproheptadine) 129-03-3, 969-33-5;
 (desipramine) 50-47-5, 58-28-6; (fluoxetine)
 54910-89-3, 56296-78-7, 59333-67-4; (fluvoxamine)
 54739-18-3; (guanfacine) 29110-47-2, 29110-48-3;
 (imipramine) 113-52-0, 50-49-7; (lithium) 7439-93-2;
 (nefazodone) 82752-99-6, 83366-66-9; (ofloxacin)
 82419-36-1; (paroxetine) 61869-08-7; (pefloxacin)
 70458-92-3; (propranolol) 13013-17-7, 318-98-9, 3506-09-0,
 4199-09-1, 525-66-6; (risperidone) 106266-06-2; (valproic
 acid) 1069-66-5, 99-66-1

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ACCESSION NUMBER: 2004314067 EMBASE Full-text
 TITLE: Microvascular complications in cystic fibrosis-related diabetes mellitus: A case report.
 AUTHOR: Scott, Andrew I.R.; Bell, Scott C. (correspondence)
 CORPORATE SOURCE: Adult Cystic Fibrosis Unit, University of Queensland, Rode Rd., Brisbane, QLD 4032, Australia. bells@health.qld.gov.au
 AUTHOR: Clarke, Belinda E.
 CORPORATE SOURCE: Department of Anatomical Pathology, The Prince Charles Hospital, Brisbane, QLD, Australia.
 AUTHOR: Healy, Helen
 CORPORATE SOURCE: Department of Renal Medicine, Royal Brisbane Hospital, Brisbane, QLD, Australia.
 AUTHOR: D'Emden, Michael
 CORPORATE SOURCE: Department of Endocrinology, Royal Brisbane Hospital, Brisbane, QLD, Australia.
 AUTHOR: Bell, Scott C. (correspondence)
 CORPORATE SOURCE: Department of Thoracic Medicine, University of Queensland, The Prince Charles Hospital, Rode Rd., Brisbane, QLD 4032, Australia. bells@health.qld.gov.au
 SOURCE: Journal of the Pancreas, (Nov 2000) Vol. 1, No. 4, pp. 208-210.
 Refs: 6
 ISSN: 1590-8577 CODEN: JPOAC6
 COUNTRY: Italy
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 003 Endocrinology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology
 006 Internal Medicine
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 5 Aug 2004
 Last Updated on STN: 5 Aug 2004

ABSTRACT: Context. The prevalence of cystic fibrosis-related diabetes mellitus is increasing and is associated with increased survival from cystic fibrosis. Case Report. This study describes a case of the premature onset of disabling and widespread microvascular complications resulting from cystic fibrosis-related diabetes mellitus. Previously asymptomatic retinopathy was diagnosed on recognition of diabetic nephropathy. Conclusions. The treatment of pulmonary exacerbations has become more complex due to the nephrotoxic

potential of intravenous aminoglycoside drugs which are frequently used to control chronic *Pseudomonas* infection in cystic fibrosis.

CONTROLLED TERM: Medical Descriptors:

adult
article
case report
*cystic fibrosis: DI, diagnosis
*cystic fibrosis: DT, drug therapy
*diabetes mellitus: CO, complication
*diabetes mellitus: DI, diagnosis
*diabetes mellitus: DT, drug therapy
*diabetes mellitus: PC, prevention
*diabetes mellitus: TH, therapy
*diabetic angiopathy: CO, complication
*diabetic angiopathy: ET, etiology
diabetic nephropathy: CO, complication
diabetic nephropathy: DI, diagnosis
diabetic nephropathy: DT, drug therapy
diabetic retinopathy: CO, complication
diabetic retinopathy: DI, diagnosis
diabetic retinopathy: TH, therapy
disease exacerbation: DT, drug therapy
female
Gram negative infection: DT, drug therapy
human
infection control
lung disease: DI, diagnosis
lung disease: DT, drug therapy
lung disease: ET, etiology
lung disease: TH, therapy
nephrotoxicity: SI, side effect
orthostatic hypotension: SI, side effect
prevalence
survival time

CONTROLLED TERM:

Drug Descriptors:
aminoglycoside: AE, adverse drug reaction
aminoglycoside: CB, drug combination
aminoglycoside: DT, drug therapy
aminoglycoside: IV, intravenous drug administration
amitriptyline: CB, drug combination
beta lactam antibiotic: CB, drug combination
beta lactam antibiotic: DT, drug therapy
ceftazidime: DT, drug therapy
diclofenac: AE, adverse drug reaction
diclofenac: CB, drug combination
insulin: DT, drug therapy
lisinopril: AE, adverse drug reaction
lisinopril: DT, drug therapy
oral antidiabetic agent: DT, drug therapy
oral antidiabetic agent: PO, oral drug administration
tobramycin: DT, drug therapy
CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (ceftazidime) 72558-82-8; (diclofenac) 15307-79-6, 15307-86-5; (insulin) 9004-10-8; (lisinopril) 76547-98-3, 83915-83-7; (tobramycin) 32986-56-4

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ACCESSION NUMBER: 2000065546 EMBASE Full-text

10/524815

TITLE: Breast disorders in the pediatric and adolescent patient.
AUTHOR: Templeman, C.; Hertweck, S.P., Dr. (correspondence)
CORPORATE SOURCE: Dept. of Obstetrics and Gynecology, University of
Louisville, 550 S Jackson St, Louisville, KY 40292, United
States.
SOURCE: Obstetrics and Gynecology Clinics of North America, (2000)
Vol. 27, No. 1, pp. 19-34.
Refs: 78
ISSN: 0889-8545 CODEN: OGCAE8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 010 Obstetrics and Gynecology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
038 Adverse Reactions Titles
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 2 Mar 2000
Last Updated on STN: 2 Mar 2000

ABSTRACT: Despite the wide range of breast abnormalities that affect patients in the pediatric and adolescent populations, some conclusions can be drawn. Breast self-examination in the adolescent population is controversial but is recommended for girls who carry the BRCA1 or BRCA2 gene beginning at age 18 to 21 years. All girls with a disorder of breast size or symmetry should be given the opportunity of consultation with a plastic surgeon to discuss reconstructive options. Ultrasound is the most appropriate initial investigation in any adolescent patient with a breast mass owing to the dense nature of breast tissue in this age group. Although it is extremely rare in this population, breast cancer must always be included in the differential diagnosis of a breast mass, particularly in the patient with a prior history of childhood malignancy or chest irradiation.

CONTROLLED TERM: Medical Descriptors:
*adolescence
adolescent
*breast cancer: DI, diagnosis
*breast cancer: EP, epidemiology
*breast cancer: ET, etiology
*breast cancer: PC, prevention
breast development
*breast disease: CN, congenital disorder
*breast disease: DI, diagnosis
*breast disease: EP, epidemiology
*breast disease: ET, etiology
*breast disease: PC, prevention
*breast disease: SI, side effect
breast examination
breast hyperplasia: DI, diagnosis
breast hyperplasia: ET, etiology
breast hyperplasia: SU, surgery
breast hypoplasia: DI, diagnosis
breast hypoplasia: ET, etiology
breast hypoplasia: SU, surgery
*breast malformation: CN, congenital disorder
*breast malformation: DI, diagnosis
*breast malformation: ET, etiology
*breast malformation: SU, surgery
cystosarcoma phylloides: DI, diagnosis
cystosarcoma phylloides: ET, etiology

cystosarcoma phylloides: SU, surgery
 female
 fibrocystic breast disease: DI, diagnosis
 fibrocystic breast disease: DT, drug therapy
 fibrocystic breast disease: ET, etiology
 galactorrhea: SI, side effect
 human
 mastitis: DI, diagnosis
 mastitis: DT, drug therapy
 mastitis: ET, etiology
 nipple malformation: CN, congenital disorder
 nipple malformation: DI, diagnosis
 nipple malformation: ET, etiology
 patient counseling
 Poland syndrome: CN, congenital disorder
 Poland syndrome: DI, diagnosis
 Poland syndrome: ET, etiology
 priority journal
 review

CONTROLLED TERM:

Drug Descriptors:
 amitriptyline: AE, adverse drug reaction
 amphetamine: AE, adverse drug reaction
 androgen: AE, adverse drug reaction
 anesthetic agent: AE, adverse drug reaction
 antibiotic agent: DT, drug therapy
 chlorpromazine: AE, adverse drug reaction
 cimetidine: AE, adverse drug reaction
 domperidone: AE, adverse drug reaction
 *estrogen: AE, adverse drug reaction
 *estrogen: DT, drug therapy
 *estrogen: PO, oral drug administration
 fluphenazine: AE, adverse drug reaction
 haloperidol: AE, adverse drug reaction
 *medroxyprogesterone acetate: DT, drug therapy
 *medroxyprogesterone acetate: PO, oral drug administration
 meprobamate: AE, adverse drug reaction
 methyl dopa: AE, adverse drug reaction
 methylxanthine
 metoclopramide: AE, adverse drug reaction
 monoamine oxidase inhibitor: AE, adverse drug reaction
 narcotic agent: AE, adverse drug reaction
 opiate: AE, adverse drug reaction
 *oral contraceptive agent: DT, drug therapy
 *oral contraceptive agent: PO, oral drug administration
 primrose oil: DO, drug dose
 primrose oil: DT, drug therapy
 prostaglandin: AE, adverse drug reaction
 reserpine: AE, adverse drug reaction
 sulpiride: AE, adverse drug reaction
 trifluoperazine: AE, adverse drug reaction
 (amitriptyline) 50-48-6, 549-18-8; (amphetamine)
 1200-47-1, 139-10-6, 156-34-3, 2706-50-5, 300-62-9,
 51-62-7, 60-13-9, 60-15-1; (chlorpromazine) 50-53-3,
 69-09-0; (cimetidine) 51481-61-9, 70059-30-2; (domperidone)
 57808-66-9; (fluphenazine) 146-56-5, 69-23-8; (haloperidol)
 52-86-8; (medroxyprogesterone acetate) 71-58-9;
 (meprobamate) 57-53-4; (methyl dopa) 555-29-3, 555-30-6;
 (methylxanthine) 28109-92-4; (metoclopramide) 12707-59-4,
 2576-84-3, 364-62-5, 7232-21-5; (opiate) 53663-61-9,
 8002-76-4, 8008-60-4; (primrose oil) 65546-85-2;

CAS REGISTRY NO.:

(reserpine) 50-55-5, 8001-95-4; (sulpiride) 15676-16-1;
(trifluoperazine) 117-89-5, 440-17-5

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ACCESSION NUMBER: 1999131082 EMBASE Full-text
TITLE: Adverse drug reactions in the urinary tract.
AUTHOR: Soomro, Naeem A. (correspondence)
CORPORATE SOURCE: Freeman Hospital, Newcastle upon Tyne NE7 7DN, United Kingdom.
AUTHOR: Neal, David E.
CORPORATE SOURCE: Medical School, University of Newcastle, Newcastle upon Tyne NE2 4HH, United Kingdom.
SOURCE: Adverse Drug Reaction Bulletin, (1998) No. 193, pp. 735-738.
Refs: 85
ISSN: 0044-6394 CODEN: ADRBBA
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 1999
Last Updated on STN: 29 Apr 1999

ABSTRACT: Drugs can cause adverse effects on the urinary tract by a local action, or as a result of systemic effects on the autonomic nervous system, or central nervous control of bladder emptying. Tiaprofenic acid and cyclophosphamide as its metabolite acrolein, for example, can cause haemorrhagic cystitis. Localised retroperitoneal fibrosis, from methysergide, for instance, can lead to hydronephrosis. Agents with anticholinergic actions, such as the tricyclic antidepressants, can result in urinary retention, whilst alpha-adrenoceptor antagonists may lead to stress incontinence in females.

CONTROLLED TERM: Medical Descriptors:
autonomic nervous system
central nervous system
cystic fibrosis: DT, drug therapy
cystitis: SI, side effect
environmental exposure
hemorrhagic cystitis: DT, drug therapy
hemorrhagic cystitis: PC, prevention
hemorrhagic cystitis: SI, side effect
human
hydronephrosis: SI, side effect
inhalational drug administration
intravenous drug administration
micturition
oral drug administration
retroperitoneal fibrosis: SI, side effect
short survey
stress incontinence: SI, side effect
*urinary tract disease: ET, etiology
*urinary tract disease: SI, side effect
urine retention: SI, side effect
CONTROLLED TERM: Drug Descriptors:
acetylcysteine: DT, drug therapy

acrolein: AE, adverse drug reaction
 allopurinol: AE, adverse drug reaction
 alpha adrenergic receptor blocking agent: AE, adverse drug reaction
 antibiotic agent: AE, adverse drug reaction
 antineoplastic agent: AE, adverse drug reaction
 busulfan: AE, adverse drug reaction
 carbenicillin: AE, adverse drug reaction
 carbenicillin: DT, drug therapy
 carmustine: AE, adverse drug reaction
 chlorambucil: AE, adverse drug reaction
 chlormethine: AE, adverse drug reaction
 cholinergic receptor blocking agent: AE, adverse drug reaction
 cyclophosphamide: AE, adverse drug reaction
 cyclophosphamide: PK, pharmacokinetics
 danazol: AE, adverse drug reaction
 drug metabolite: AE, adverse drug reaction
 ether: AE, adverse drug reaction
 isoniazid: AE, adverse drug reaction
 mesna: AD, drug administration
 mesna: DT, drug therapy
 methenamine mandelate: AE, adverse drug reaction
 methysergide: AE, adverse drug reaction
 meticillin: AE, adverse drug reaction
 nafcillin: AE, adverse drug reaction
 penicillin G: AE, adverse drug reaction
 piperacillin: AE, adverse drug reaction
 piperacillin: DT, drug therapy
 spasmolytic agent: AE, adverse drug reaction
 tiaprofenic acid: AE, adverse drug reaction
 ticarcillin: AE, adverse drug reaction
 ticarcillin: DT, drug therapy
 tricyclic antidepressant agent: AE, adverse drug reaction
 unindexed drug: AE, adverse drug reaction
 vincristine: AE, adverse drug reaction

CAS REGISTRY NO.: (acetylcysteine) 616-91-1; (acrolein) 107-02-8;
 (allopurinol) 315-30-0; (busulfan) 55-98-1; (carbenicillin)
 17230-86-3, 4697-36-3, 4800-94-6; (carmustine) 154-93-8;
 (chlorambucil) 305-03-3; (chlormethine) 51-75-2, 55-86-7,
 82905-71-3; (cyclophosphamide) 50-18-0; (danazol)
 17230-88-5; (ether) 60-29-7; (isoniazid) 54-85-3,
 62229-51-0, 65979-32-0; (mesna) 19767-45-4, 3375-50-6;
 (methenamine mandelate) 587-23-5; (methysergide)
 16509-15-2, 361-37-5, 62288-72-6; (meticillin) 132-92-3,
 38882-79-0, 61-32-5; (nafcillin) 147-52-4, 985-16-0;
 (penicillin G) 1406-05-9, 61-33-6; (piperacillin)
 59703-84-3, 61477-96-1; (tiaprofenic acid) 33005-95-7;
 (ticarcillin) 29457-07-6, 34787-01-4, 4697-14-7;
 (vincristine) 57-22-7

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ACCESSION NUMBER: 1998246165 EMBASE Full-text
 TITLE: Male breast disease.
 AUTHOR: Gateley, C.A. (correspondence)
 CORPORATE SOURCE: Royal Gwent Hospital, Newport NP9 2UB, United Kingdom.
 SOURCE: Breast, (Jun 1998) Vol. 7, No. 3, pp. 121-127.
 Refs: 45
 ISSN: 0960-9776 CODEN: BREAEK

10/524815

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
006 Internal Medicine

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 6 Aug 1998

Last Updated on STN: 6 Aug 1998

ABSTRACT: A variety of benign and malignant breast conditions affect the male breast. Gynaecomastia is common in puberty and old age and only when it is progressive or presents outwith these age groups are specific investigations indicated. Male breast cancer accounts for approximately 0.7% of all breast cancers. Lifetime risk for a male with an affected mother and sister is 2.3% and some of the families carry the BRCA2 gene. Infection is uncommon but when it does occur, causes include smoking in periareolar sepsis.

CONTROLLED TERM: Medical Descriptors:
alcoholism: ET, etiology
breast cancer: DT, drug therapy
breast cancer: EP, epidemiology
breast cancer: ET, etiology
breast cancer: RT, radiotherapy
breast cancer: SU, surgery
*breast disease: DT, drug therapy
*breast disease: EP, epidemiology
*breast disease: ET, etiology
*breast disease: RT, radiotherapy
*breast disease: SI, side effect
*breast disease: SU, surgery
clinical examination
drug effect
fibrocystic breast disease: ET, etiology
fibrocystic breast disease: TH, therapy
gynecomastia: DT, drug therapy
gynecomastia: ET, etiology
gynecomastia: SI, side effect
gynecomastia: SU, surgery
human
hyperthyroidism: ET, etiology
infection: CO, complication
infection: DT, drug therapy
infection: SU, surgery
kidney failure: ET, etiology
klinefelter syndrome: CN, congenital disorder
liver failure: ET, etiology
male
male breast
mother
nipple malformation: CO, complication
priority journal
puberty
radiotherapy
review
senescence
smoking
starvation
surgery

testis disease: ET, etiology
 Drug Descriptors:
 amiloride: AE, adverse drug reaction
 anabolic agent: AE, adverse drug reaction
 androgen: EC, endogenous compound
 antiandrogen: AE, adverse drug reaction
 antiinfective agent: AE, adverse drug reaction
 captopril: AE, adverse drug reaction
 clonidine: AE, adverse drug reaction
 danazol: DT, drug therapy
 domperidone: AE, adverse drug reaction
 estrogen: EC, endogenous compound
 ethionamide: AE, adverse drug reaction
 furosemide: AE, adverse drug reaction
 ibuprofen: AE, adverse drug reaction
 isoniazid: AE, adverse drug reaction
 methyldopa: AE, adverse drug reaction
 metoclopramide: AE, adverse drug reaction
 metronidazole: AE, adverse drug reaction
 nifedipine: AE, adverse drug reaction
 phenothiazine: AE, adverse drug reaction
 sex hormone: AE, adverse drug reaction
 tamoxifen: DT, drug therapy
 testosterone: AE, adverse drug reaction
 theophylline: AE, adverse drug reaction
 tricyclic antidepressant agent: AE, adverse drug reaction
 verapamil: AE, adverse drug reaction

CAS REGISTRY NO.:
 (amiloride) 2016-88-8, 2609-46-3; (captopril) 62571-86-2;
 (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (danazol)
 17230-88-5; (domperidone) 57808-66-9; (ethionamide)
 536-33-4; (furosemide) 54-31-9; (ibuprofen) 15687-27-1;
 (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (methyldopa)
 555-29-3, 555-30-6; (metoclopramide) 12707-59-4, 2576-84-3,
 364-62-5, 7232-21-5; (metronidazole) 39322-38-8, 443-48-1;
 (nifedipine) 21829-25-4; (phenothiazine) 92-84-2;
 (tamoxifen) 10540-29-1; (testosterone) 58-22-0;
 (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1,
 99007-19-9; (verapamil) 152-11-4, 52-53-9

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ACCESSION NUMBER: 1997008554 EMBASE [Full-text](#)
 TITLE: The pathobiology of biliary epithelia.
 AUTHOR: Roberts, S.K.; Ludwig, J.; LaRusso, N.F., Dr.
 (correspondence)
 CORPORATE SOURCE: Basic Res. in Digestive Dis. Ctr., Mayo Medical School,
 Clinic and Foundation, 200 First Street Southwest,
 Rochester, MN 55905, United States.
 SOURCE: Gastroenterology, (1997) Vol. 112, No. 1, pp. 269-279.
 Refs: 63
 ISSN: 0016-5085 CODEN: GASTAB
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 037 Drug Literature Index
 038 Adverse Reactions Titles
 048 Gastroenterology

LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 28 Jan 1997
 Last Updated on STN: 28 Jan 1997

ABSTRACT: Our understanding of the pathobiology of biliary epithelia is rapidly growing because of a surge of investigative activity. This became possible after suitable experimental models and techniques were developed with which to study cholangiocyte biology. Although the molecular mechanisms of bile formation by cholangiocytes and the role of these cells as a major cellular target in a variety of severe hepatobiliary diseases are currently being investigated, many questions remain unanswered, particularly regarding cholangiocellular functions, both in normal and abnormal conditions. As current experimental models become more refined, scientists with interests as diverse as cell biology and physiology, morphology, pharmacology, immunology, genetics, and oncology can be expected to further clarify the pathobiology of biliary epithelia.

CONTROLLED TERM: Medical Descriptors:
 acquired immune deficiency syndrome
 animal cell
 animal model
 bile duct carcinoma: ET, etiology
 *bile duct disease: ET, etiology
 *bile duct disease: SI, side effect
 biliary tract infection: ET, etiology
 cystic fibrosis: ET, etiology
 drug induced disease: ET, etiology
 drug induced disease: SI, side effect
 experimental model
 human
 human cell
 nonhuman
 pathophysiology
 primary sclerosing cholangitis: ET, etiology
 priority journal
 rat
 review

CONTROLLED TERM: Drug Descriptors:
 amitriptyline: AE, adverse drug reaction
 amoxicillin: AE, adverse drug reaction
 ampicillin: AE, adverse drug reaction
 carbamazepine: AE, adverse drug reaction
 chlorpromazine: AE, adverse drug reaction
 cromoglycate disodium: AE, adverse drug reaction
 cyproheptadine: AE, adverse drug reaction
 diazepam: AE, adverse drug reaction
 erythromycin: AE, adverse drug reaction
 haloperidol: AE, adverse drug reaction
 imipramine: AE, adverse drug reaction
 methyltestosterone: AE, adverse drug reaction
 paracetamol: AE, adverse drug reaction
 phenylbutazone: AE, adverse drug reaction
 prochlorperazine: AE, adverse drug reaction
 tiabendazole: AE, adverse drug reaction
 tolbutamide: AE, adverse drug reaction
 trifluoperazine: AE, adverse drug reaction
 troleandomycin: AE, adverse drug reaction

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (amoxicillin) 26787-78-0, 34642-77-8, 61336-70-7; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (carbamazepine) 298-46-4, 8047-84-5; (chlorpromazine) 50-53-3, 69-09-0; (cromoglycate disodium) 15826-37-6, 16110-51-3, 93356-79-7, 93356-84-4; (cyproheptadine) 129-03-3, 969-33-5; (diazepam) 439-14-5; (erythromycin) 114-07-8, 70536-18-4;

(haloperidol) 52-86-8; (imipramine) 113-52-0,
 50-49-7; (methyltestosterone) 58-18-4; (paracetamol)
 103-90-2; (phenylbutazone) 129-18-0, 50-33-9, 8054-70-4;
 (prochlorperazine) 58-38-8; (tiabendazole) 148-79-8;
 (tolbutamide) 473-41-6, 64-77-7; (trifluoperazine)
 117-89-5, 440-17-5; (troleandomycin) 2751-09-9

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ACCESSION NUMBER: 1998019436 EMBASE Full-text
 TITLE: Obstetric issues in women with neurologic diseases.
 AUTHOR: Norwitz, E.R., Dr. (correspondence); Repke, J.T.
 CORPORATE SOURCE: Department of Obstetrics/Gynecology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States
 SOURCE: Current Problems in Obstetrics, Gynecology and Fertility, (1997) Vol. 20, No. 6, pp. 190-230.
 Refs: 279
 ISSN: 8756-0410 CODEN: CPOIEN
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 010 Obstetrics and Gynecology
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 008 Neurology and Neurosurgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 2 Feb 1998
 Last Updated on STN: 2 Feb 1998

ABSTRACT: During pregnancy, the investigation and management of neurologic conditions is complicated by concern about the safety of the fetus. This manuscript is designed as a clinical reference for the practicing obstetrician. It will focus on the management of late pregnancy, labor, and delivery in patients with specific neurologic ailments. A systematic, anatomic approach has been taken. The review starts with a discussion of neurologic diseases of the brain and works its way down the spinal cord and peripheral nerves, across the neuromuscular junctions to the muscles. Movement disorders are considered separately. The monograph concludes with discussions of neurologic emergencies during pregnancy, as well as other situations specific to obstetric practice (such as drugs and breast-feeding, genetic counseling, and antenatal diagnosis for inherited neurologic diseases.) Disorders of the Brain includes discussions about the incidence, differential diagnosis, and management of a number of clinical conditions that center on the brain. These include headache; seizure disorders (focusing on management issues during pregnancy and implications for the fetus and newborn); cerebrovascular disease (stroke, Sheehan's syndrome, hypertensive encephalopathy); and demyelinating and degenerating diseases (multiple sclerosis, Huntington's disease). Infections of the nervous system (syphilis, polio, tetanus, toxoplasmosis, Lyme disease, HIV) occur in pregnancy, as they do in the nonpregnant state, but diagnosis and management might be different. The effects of inflammatory conditions of the central nervous system and intracranial tumors on pregnancy are reviewed briefly. There is a separate discussion about radiation exposure and its effects on the developing fetus. This discussion concludes that, in general, the use of radiographic technology (either diagnostic or therapeutic), if indicated, should not be restricted because the patient is pregnant. Psychiatric disorders affecting pregnancy (those that precede pregnancy, as well as conditions that result from pregnancy—such as postpartum depression and psychosis) often are overlooked. The warning signs and treatment of such conditions are discussed in detail. Disorders of the Spinal Cord includes discussions about specific topics (such as pregnancy in women with spinal-cord

injuries and the entity of autonomic dysreflexia), as well as some more general topics (such as backache in pregnancy). Disorders of Peripheral Nerves covers both mononeuropathies (carpal tunnel syndrome, Bell's palsy, meralgia paresthetica) and polyneuropathies (Guillain-Barre syndrome, porphyric neuropathy, and the hereditary polyneuropathies). The 'lithotomy' position derives its name from Greek 'lithos,' meaning stone, and 'otomy,' meaning to cut. It is so named because it was the position in which elderly men were placed for surgical removal of obstructing bladder stones. It is not a natural position for childbirth and might create nerve injury as the result of compression and/or stretching of a particular peripheral nerve of nerve plexus. Symptoms of such obstetric neuropathies are usually mild and unilateral, and complete recovery can be expected in the majority of cases. These are reviewed in greater detail. Disorders of the Neuromuscular Junction focuses on myasthenia gravis, its effect on pregnancy, implications for the fetus and newborn, and management during labor and delivery. Disorders of Muscle includes brief discussions about muscle cramping and a number of specific muscular disorders, such as myotonic dystrophy, myotonia congenita, and polymyositis/dermatomyositis. Movement disorders are considered separately. These include a definition of some of the generalized involuntary movements, with specific reference to chorea gravidarum and Wilson's disease. Localized involuntary movements are discussed briefly, including the 'restless leg syndrome,' which is reputed to be the most common movement disorder in pregnancy. It usually occurs in the third trimester and has been reported in up to 11% to 12% of all pregnancies. Neurologic Emergencies During Pregnancy reviews the management of such conditions as status epilepticus and disorders of consciousness (coma) during pregnancy and delivery. Miscellaneous Neurologic Conditions Specific to Pregnancy includes such topics as neurologic birth injury (intracranial hemorrhage, brachial-plexus injury, fetal acidosis, cerebral palsy) and other congenital neurologic injuries (facial nerve paralysis, injuries to the neck and spine, multicystic encephalomalacia). Many factors might put a fetus at risk for a genetic disorder or neurologic birth defect. The section Neurologic Disorders in the Fetus explores the need for comprehensive genetic counseling both before and after conception. A number of preventative measures are outlined. They might ameliorate the risk of congenital neurologic anomaly, such as meticulous periconceptional glucose control in women with insulin-dependent diabetes, folic acid supplementation for women who have had a previous fetus with neural-tube defect, and parental karyotyping for couples at risk of having a fetus with one of the more common autosomal recessive disorders (Tay-Sachs disease, cystic fibrosis, sickle cell anemia). Recommendations for routine prenatal screening (including maternal serum alpha-fetoprotein, triple-panel serum screening, ultrasonography, and amniocentesis and other fetal genetic testing) are reviewed in detail. The section ends with a detailed discussion on drugs and breast-feeding. In general, most chronic neurologic disorders are compatible with normal pregnancy outcome. Diagnostic investigations (including imaging studies) and treatment protocols should be initiated, if indicated. The implications of such interventions for the developing fetus, however, should not be overlooked.

CONTROLLED TERM: Medical Descriptors:
 birth injury
 brain infection: DI, diagnosis
 brain tumor: DI, diagnosis
 cerebrovascular disease: DI, diagnosis
 coma
 degenerative disease: DI, diagnosis
 delivery
 demyelinating disease: DI, diagnosis
 diagnostic imaging
 differential diagnosis

epileptic state
 female
 fetus disease
 genetic counseling
 headache: DI, diagnosis
 headache: DT, drug therapy
 human
 intravenous drug administration
 labor
 mental disease: DT, drug therapy
 migraine: DI, diagnosis
 migraine: DT, drug therapy
 motor dysfunction: DI, diagnosis
 myopathy: DI, diagnosis
 *neurologic disease
 neuromuscular junction disorder: DI, diagnosis
 *obstetrics
 peripheral neuropathy: DI, diagnosis
 pregnancy
 prenatal diagnosis
 review
 seizure: DI, diagnosis
 seizure: DT, drug therapy
 spinal cord disease: DI, diagnosis
 Drug Descriptors:
 amitriptyline: DT, drug therapy
 *anticonvulsive agent: DT, drug therapy
 *anticonvulsive agent: TO, drug toxicity
 *antimigraine agent: DT, drug therapy
 anxiolytic agent: DT, drug therapy
 carbamazepine: DT, drug therapy
 carbamazepine: TO, drug toxicity
 clomethiazole: DT, drug therapy
 clomipramine: DT, drug therapy
 clonazepam: DT, drug therapy
 clonazepam: TO, drug toxicity
 desipramine: DT, drug therapy
 diazepam: DT, drug therapy
 doxepin: DT, drug therapy
 ethosuximide: DT, drug therapy
 ethosuximide: TO, drug toxicity
 felbamate: DT, drug therapy
 felbamate: TO, drug toxicity
 fluoxetine: DT, drug therapy
 gabapentin: DT, drug therapy
 gabapentin: TO, drug toxicity
 imipramine: DT, drug therapy
 klonipin
 lamotrigine: DT, drug therapy
 lamotrigine: TO, drug toxicity
 magnesium sulfate: DT, drug therapy
 monoamine oxidase inhibitor: DT, drug therapy
 neuroleptic agent: DT, drug therapy
 nortriptyline: DT, drug therapy
 phenobarbital: DT, drug therapy
 phenobarbital: TO, drug toxicity
 phenytoin: DT, drug therapy
 phenytoin: TO, drug toxicity
 primidone: DT, drug therapy
 primidone: TO, drug toxicity

CONTROLLED TERM:

*psychotropic agent: DT, drug therapy
 serotonin uptake inhibitor: DT, drug therapy
 tricyclic antidepressant agent: DT, drug therapy
 trimethadione: DT, drug therapy
 trimethadione: TO, drug toxicity
 unclassified drug
 unindexed drug
 valproic acid: DT, drug therapy
 valproic acid: TO, drug toxicity

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (carbamazepine) 298-46-4, 8047-84-5; (clomethiazole) 1867-58-9, 533-45-9; (clomipramine) 17321-77-6, 303-49-1; (clonazepam) 1622-61-3; (desipramine) 50-47-5, 58-28-6; (diazepam) 439-14-5; (doxepin) 1229-29-4, 1668-19-5; (ethosuximide) 77-67-8; (felbamate) 25451-15-4; (fluoxetine) 54910-89-3, 56296-78-7, 59333-67-4; (gabapentin) 60142-96-3; (imipramine) 113-52-0, 50-49-7; (lamotrigine) 84057-84-1; (magnesium sulfate) 7487-88-9; (nortriptyline) 72-69-5, 894-71-3; (phenobarbital) 50-06-6, 57-30-7, 8028-68-0; (phenytoin) 57-41-0, 630-93-3; (primidone) 125-33-7; (trimethadione) 127-48-0; (valproic acid) 1069-66-5, 99-66-1

CHEMICAL NAME: adapin; anafranil; depakene; dilantin; elavil; felbatol; klonopin; lamictal; luminal; mysoline; neurontin; norpramin; pamelor; prozac; tegretol; tofranil; tridione; zartotin

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ACCESSION NUMBER: 1996337659 EMBASE [Full-text](#)

TITLE: Use of a rapid HPLC assay for determination of pharmacokinetic parameters of ibuprofen in patients with cystic fibrosis.

AUTHOR: Rifai, Nader (correspondence); Sakamoto, Masayuki; Law, Terence; Galpchian, Vartouhi; Harris, Neil

CORPORATE SOURCE: Department of Laboratory Medicine, Children's Hospital, Harvard Medical School, Boston, MA, United States. rifai@al.tch.harvard.edu

AUTHOR: Rifai, Nader (correspondence); Harris, Neil

CORPORATE SOURCE: Department of Pathology, Children's Hospital, Harvard Medical School, Boston, MA, United States. rifai@al.tch.harvard.edu

AUTHOR: Colin, Andrew A.

CORPORATE SOURCE: Department of Medicine, Children's Hospital, Harvard Medical School, Boston, MA, United States.

AUTHOR: Rifai, Nader (correspondence)

CORPORATE SOURCE: Children's Hospital, Department of Laboratory Medicine, 300 Longwood Ave., Boston, MA 02115, United States. rifai@al.tch.harvard.edu

AUTHOR: Rifai, Nader (correspondence)

CORPORATE SOURCE: Department of Laboratory Medicine, Children's Hospital, 300 Longwood Ave., Boston, MA 02115, United States.

SOURCE: Clinical Chemistry, (1996) Vol. 42, No. 11, pp. 1812-1816. Refs: 17

ISSN: 0009-9147 CODEN: CLCHAU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index

LANGUAGE: English

10/524815

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1996
Last Updated on STN: 3 Dec 1996

ABSTRACT: High doses of ibuprofen have been shown to delay the progression of lung disease without serious adverse effects in patients with cystic fibrosis. To be effective, peak ibuprofen concentration of 50 to 100 mg/L has to be achieved. We developed an HPLC assay to rapidly determine plasma ibuprofen concentration. We used this assay to determine the pharmacokinetics of ibuprofen in patients with cystic fibrosis. The assay possessed linearity up to 500 mg/L, sensitivity to 1 mg/L, average recovery of 98%, and run-to-run precision (n = 23) of 3%. Furthermore, the assay proved to be free of interference from 51 medications. Observed time to peak concentration varied significantly between those receiving ibuprofen tablets (mean + SD, 94 ± 29 min, n = 16) and syrup (30 ± 0 min, n = 4) (P < 0.0001). We conclude that the method described here is ideal for therapeutic monitoring of ibuprofen.

CONTROLLED TERM: Medical Descriptors:
adolescent
adult
article
child
clinical article
clinical trial
*cystic fibrosis: CN, congenital disorder
disease course
drug absorption
drug blood level
drug determination
drug formulation
drug half life
drug monitoring
female
human
*inflammation
male
oral drug administration
reversed phase high performance liquid chromatography

CONTROLLED TERM: Drug Descriptors:
acecainide
acetylsalicylic acid
amikacin
amitriptyline
*antiarrhythmic agent
antibiotic agent
*anticonvulsive agent
*antidepressant agent
*antiinflammatory agent
brompheniramine
caffeine
cefazolin
clonazepam
clotrimazole
digitoxin
digoxin
disopyramide
doxepin
felbamate
ibufenac
*ibuprofen: CT, clinical trial

*ibuprofen: AD, drug administration
 *ibuprofen: AN, drug analysis
 *ibuprofen: CR, drug concentration
 *ibuprofen: PR, pharmaceuticals
 *ibuprofen: PK, pharmacokinetics
 imipenem
 ketoprofen
 lidocaine
 metharbital
 paracetamol
 phenytoin
 *propionic acid derivative
 tobramycin
 unindexed drug

CAS REGISTRY NO.: (acecainide) 32795-44-1, 34118-92-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (amikacin) 37517-28-5, 39831-55-5; (amitriptyline) 50-48-6, 549-18-8; (brompheniramine) 86-22-6, 980-71-2; (caffeine) 30388-07-9, 58-08-2; (cefazolin) 25953-19-9, 27164-46-1; (clonazepam) 1622-61-3; (clotrimazole) 23593-75-1; (digitoxin) 71-63-6; (digoxin) 20830-75-5, 57285-89-9; (disopyramide) 3737-09-5; (doxepin) 1229-29-4, 1668-19-5; (felbamate) 25451-15-4; (ibufenac) 1553-60-2; (ibuprofen) 15687-27-1; (imipenem) 64221-86-9; (ketoprofen) 22071-15-4, 57495-14-4; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (metharbital) 50-11-3; (paracetamol) 103-90-2; (phenytoin) 57-41-0, 630-93-3; (tobramycin) 32986-56-4

CHEMICAL NAME:

(1) motrin

COMPANY NAME:

(1) upjohn (United States); sigma (United States)

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ACCESSION NUMBER: 1996212929 EMBASE Full-text

TITLE: Obstructive lung disease and sleep.

AUTHOR: Jokic, R.; Fitzpatrick, M.F., Dr. (correspondence)

CORPORATE SOURCE: Department of Medicine, University of Saskatchewan, Royal University Hospital, Saskatoon, Sask. S7N 0X0, Canada.

SOURCE: Medical Clinics of North America, (1996) Vol. 80, No. 4, pp. 821-850.

ISSN: 0025-7125 CODEN: MCNAAG

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

037 Drug Literature Index

006 Internal Medicine

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Aug 1996

Last Updated on STN: 14 Aug 1996

ABSTRACT: There is a significant interaction between obstructive lung disease and sleep-sleep is associated with clinical deterioration in obstructive lung disease, and vice versa. Knowledge of the pathophysiology of deterioration in obstructive lung disease during sleep is essential to the understanding of the management of this problem. Recent information has helped clarify this pathophysiology and has led to more aggressive treatment for deterioration of obstructive lung disease during sleep. Whether this newer and more aggressive treatment strategy improves survival or morbidity in these conditions is a challenge for future research.

CONTROLLED TERM: Medical Descriptors:
 alcohol consumption
 breathing pattern
 *chronic obstructive lung disease: DT, drug therapy
 *chronic obstructive lung disease: TH, therapy
 *cystic fibrosis: TH, therapy
 functional residual capacity
 human
 *hypoxemia: CO, complication
 oxygen therapy
 positive end expiratory pressure
 priority journal
 review
 *sleep
 *sleep apnea syndrome: DT, drug therapy
 *sleep apnea syndrome: TH, therapy

CONTROLLED TERM: Drug Descriptors:
 *acetazolamide: DT, drug therapy
 *almitrine: DO, drug dose
 *almitrine: DT, drug therapy
 *gestagen: DT, drug therapy
 *hypnotic sedative agent: DT, drug therapy
 *protriptyline: DT, drug therapy
 *theophylline: DT, drug therapy

CAS REGISTRY NO.: (acetazolamide) 1424-27-7, 59-66-5; (almitrine) 27469-53-0;
 (protriptyline) 1225-55-4, 438-60-8; (theophylline)
 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9

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ACCESSION NUMBER: 1996321652 EMBASE Full-text
 TITLE: Chronic pain in cystic fibrosis.
 AUTHOR: Ravilly, S.; Robinson, W.; Suresh, S.; Wohl, M.E.; Berde, C.B., Dr. (correspondence)
 CORPORATE SOURCE: Pain Treatment Service, Department of Anesthesia, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, United States.
 SOURCE: Pediatrics, (1996) Vol. 98, No. 4, pp. 741-747.
 ISSN: 0031-4005 CODEN: PEDIAU
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 024 Anesthesiology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 006 Internal Medicine
 007 Pediatrics and Pediatric Surgery

LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 12 Nov 1996
 Last Updated on STN: 12 Nov 1996

ABSTRACT: Objective. The objective of this study was to examine the incidence and therapy of chronic pain in a group of older patients with cystic fibrosis (CF). Patients. We identified two groups of patients followed at the CF Center at Children's Hospital (Boston); the first group consisted of all patients above the age of 5 years who died between 1984 and 1993, and the second was a cohort of 23 additional CF patients who had been referred to the Pain Treatment Service. Design. Medical charts were reviewed for the etiology and therapy of all pain episodes requiring medical intervention. Results. The incidence of chronic pain in this population increased sharply in the last 6 months of life. Headaches (55% of patients) and chest pain (65%) were

frequently reported, although back pain (19%), abdominal pain (19%), and limb pain (16%) were also reported. In patients with headache, the main etiologies were hypercarbia or hypoxia, migraine, and sinusitis. The majority of chest pain was musculoskeletal, with pleuritis, pneumothorax, and rib fracture also reported as the cause of chest pain. Interventions. A variety of nonpharmacological and pharmacological therapies were reported. Forty-one patients (53%) had pain severe enough to require opioid treatment, and 10 patients (13%) received opioids for more than 3 months. In eight patients with more severe pain, regional analgesia was found to be particularly effective. Conclusions. Chronic pain is a common problem in CF, particularly as the patient population ages. When administered with caution, opioids have proven to be effective and safe in this population; regional anesthesia can be used to preserve pulmonary toilet while adequately treating severe pain.

CONTROLLED TERM: Medical Descriptors:
 abdominal pain
 acupuncture
 adolescent
 adult
 article
 backache
 bleeding: SI, side effect
 *chronic pain: DT, drug therapy
 *chronic pain: TH, therapy
 *cystic fibrosis: CN, congenital disorder
 female
 headache
 human
 hypercapnia
 hypoxia
 major clinical study
 male
 migraine
 nerve stimulation
 pleurisy
 pneumothorax
 priority journal
 rib fracture
 school child
 sinusitis
 thorax epidural anesthesia
 thorax pain

CONTROLLED TERM: Drug Descriptors:
 ketorolac: DT, drug therapy
 *morphine: DT, drug therapy
 *nonsteroid antiinflammatory agent: AE, adverse drug reaction
 *nonsteroid antiinflammatory agent: DT, drug therapy
 *opiate: DT, drug therapy
 salazosulfapyridine: DT, drug therapy
 sumatriptan: DT, drug therapy
 trazodone: DT, drug therapy
 tricyclic antidepressant agent: DT, drug therapy

CAS REGISTRY NO.: (ketorolac) 74103-06-3; (morphine) 52-26-6, 57-27-2;
 (opiate) 53663-61-9, 8002-76-4, 8008-60-4;
 (salazosulfapyridine) 599-79-1; (sumatriptan) 103628-46-2;
 (trazodone) 19794-93-5, 25332-39-2

10/524815

ACCESSION NUMBER: 1996011372 EMBASE Full-text
TITLE: Persistent visceral pain in adolescents.
AUTHOR: Zeltzer, Lonnie, Dr. (correspondence); Koh, Jeffrey;
Hamilton, Alison
CORPORATE SOURCE: Depts. of Pediat. and Anesthesiology, Harbor-UCLA Medical
Center, University of California, Los Angeles, CA, United
States.
AUTHOR: Hyman, Paul
CORPORATE SOURCE: Department of Pediatrics, Harbor-UCLA Medical Center,
University of California, Los Angeles, CA, United States.
AUTHOR: Heyman, Melvin
CORPORATE SOURCE: Division of Gastroenterology, Department of Pediatrics,
Univ. of California at San Francisco, San Francisco, CA,
United States.
AUTHOR: Boyce, W. Thomas
CORPORATE SOURCE: Division of Behavioral Pediatrics, Department of
Pediatrics, Univ. of California at San Francisco, San
Francisco, CA, United States.
AUTHOR: Zwass, Maurice
CORPORATE SOURCE: Department of Anesthesiology, Univ. of California at San
Francisco, San Francisco, CA, United States.
AUTHOR: Feldman, Edward J.
CORPORATE SOURCE: Department of Medicine, Cedars-Sinai Medical Center, Univ.
of California at Los Angeles, Los Angeles, CA, United
States.
AUTHOR: Zeltzer, Lonnie, Dr. (correspondence)
CORPORATE SOURCE: Department of Pediatrics, UCLA School of Medicine, 22-464
MCC, 10833 LeConte Ave., Los Angeles, CA 90024-1752,
United States.
SOURCE: Journal of Pediatric Gastroenterology and Nutrition, (1996)
Vol. 22, No. 1, pp. 92-98.
Refs: 10
ISSN: 0277-2116 CODEN: JPGND6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
007 Pediatrics and Pediatric Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1996
Last Updated on STN: 30 Jan 1996
CONTROLLED TERM: Medical Descriptors:
adolescent
anorexia
article
case report
colon resection
cystic fibrosis: CN, congenital disorder
diarrhea
dose response
*enteritis: DT, drug therapy
*enteritis: SU, surgery
*hiccup
human
human tissue
hypnosis
male
nausea: DT, drug therapy
priority journal
*visceral pain: DT, drug therapy

CONTROLLED TERM: *visceral pain: TH, therapy
Drug Descriptors:
amitriptyline
*bupivacaine: DO, drug dose
*bupivacaine: DT, drug therapy
carbamazepine
cisapride
clonidine
desipramine
erythromycin
ibuprofen
*lidocaine: DT, drug therapy
lorazepam
*opiate: DT, drug therapy
prednisone: DO, drug dose
prednisone: DT, drug therapy
promethazine: DT, drug therapy
ranitidine
ranitidine

CAS REGISTRY NO.: (amitriptyline) 50-48-6, 549-18-8; (bupivacaine) 18010-40-7, 2180-92-9, 55750-21-5; (carbamazepine) 298-46-4, 8047-84-5; (cisapride) 81098-60-4; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (desipramine) 50-47-5, 58-28-6; (erythromycin) 114-07-8, 70536-18-4; (ibuprofen) 15687-27-1; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (lorazepam) 846-49-1; (opiate) 53663-61-9, 8002-76-4, 8008-60-4; (prednisone) 53-03-2; (promethazine) 58-33-3, 60-87-7; (ranitidine) 66357-35-5, 66357-59-3

CHEMICAL NAME: ativan; tegretol

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ACCESSION NUMBER: 1996009696 EMBASE Full-text
TITLE: Iontophoresis for enhancing penetration of dermatologic and antiviral drugs.
AUTHOR: Gangarosa Sr., L.P. (correspondence); Ozawa, A.; Ohkido, M.; Shimomura, Y.; Hill, J.M.
CORPORATE SOURCE: Dept. of Oral Biology-Pharmacology, School of Dentistry, Medical College of Georgia, Augusta, GA 30912-1128, United States.
SOURCE: Journal of Dermatology, (1995) Vol. 22, No. 11, pp. 865-875.
ISSN: 0385-2407 CODEN: JDMYAG
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 013 Dermatology and Venereology
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1996
Last Updated on STN: 30 Jan 1996

ABSTRACT: Iontophoresis is the process of introducing ionic drugs into the body for therapeutic purposes. Although iontophoresis has the potential for systemic therapy, it has mainly been used for local therapy at body surfaces. Many ionic drugs are available including lidocaine, epinephrine, methylprednisolone succinate, dexamethasone phosphate, several antivirals, various antibiotics, and other specific drugs. The use of an indicated ionic drug by iontophoresis offers a broad potential for promoting the development of more effective therapies in dermatology. Iontophoresis of ionized drugs

provided a 20-60 fold increase in penetration over topical application. Iontophoresis for dermatological use requires that: a) a charged drug be placed at an electrode having a polarity the same charge as the drug, b) the condition or disease under treatment be at or near the body surface, and c) a modern, sophisticated source of direct current, with appropriate accessories, be used. The current source must have features that make it not only effective, but also safe for application to the patient. Modern systems for application of drugs by iontophoresis have features that make the process simple and efficient for use in practice. Iontophoresis has a long history of use, having been suggested for various therapies for many years in medicine, physical therapy and dentistry. Pilocarpine iontophoresis is a preferred method for cystic fibrosis detection. Also, lidocaine iontophoresis has been advocated to anesthetize the tympanic membrane before myringotomy. Anesthesia of the skin to a depth of 1.0 cm or more has been reported in double-blind studies of human volunteers. Local anesthesia by iontophoresis was reported to be effective for: 1) cutaneous outcrops in patients requiring kidney dialysis, 2) delicate eyelid surgery, as the sole anesthetic, 3) preinjection topical anesthesia, and 4) shave biopsies of skin lesions. The use of iontophoresis for treating difficult cases of hyperhidrosis is quite popular among dermatologists. The present report emphasizes uses of iontophoresis in dermatology and is divided into discussion of studies using iontophoresis for postherpetic neuralgia, local anesthesia, antiviral therapy, and for corticosteroid therapy of nonspecific inflammatory lesions. Over 1250 patients have been treated for postherpetic neuralgia by corticosteroid iontophoresis at 6 medical centers with 60-80% of patients showing a major therapeutic response with return to a tolerable pain level. Double-blind studies of varicella zoster (active and postherpetic) and herpes simplex have proven that iontophoresis is a valuable modality for treating vital diseases of the skin. Many other uses for iontophoresis have been proposed in the literature that involves several hundred research papers, several textbooks and many book chapters. Review of the literature supports the concept that iontophoresis provides an optimal method for drug application in therapy of surface tissues.

CONTROLLED TERM: Medical Descriptors:
 burn: CO, complication
 clinical trial
 conference paper
 corticosteroid therapy
 drug penetration
 herpes labialis: DT, drug therapy
 *herpes simplex: DI, diagnosis
 *herpes simplex: DT, drug therapy
 *herpes zoster: DI, diagnosis
 *herpes zoster: DT, drug therapy
 human
 intravenous drug administration
 *iontophoresis
 local anesthesia
 nonhuman
 oral drug administration
 *postherpetic neuralgia: DI, diagnosis
 *postherpetic neuralgia: DT, drug therapy
 topical drug administration

CONTROLLED TERM: Drug Descriptors:
 aciclovir: AD, drug administration
 aciclovir: DT, drug therapy
 aciclovir: PR, pharmaceuticals
 amitriptyline: CB, drug combination
 amitriptyline: DT, drug therapy
 antidepressant agent: CB, drug combination

antidepressant agent: DT, drug therapy
 *antivirus agent: AD, drug administration
 *antivirus agent: DT, drug therapy
 *antivirus agent: PR, pharmaceuticals
 carbamazepine: AD, drug administration
 carbamazepine: DT, drug therapy
 carbamazepine: PR, pharmaceuticals
 *corticosteroid: AD, drug administration
 *corticosteroid: DT, drug therapy
 *corticosteroid: PR, pharmaceuticals
 idoxuridine: AD, drug administration
 idoxuridine: DT, drug therapy
 idoxuridine: PR, pharmaceuticals
 lidocaine: AD, drug administration
 lidocaine: DT, drug therapy
 lidocaine: PR, pharmaceuticals
 methylprednisolone sodium succinate: AD, drug administration
 methylprednisolone sodium succinate: DT, drug therapy
 methylprednisolone sodium succinate: PR, pharmaceuticals
 naproxen: AD, drug administration
 naproxen: CB, drug combination
 naproxen: DT, drug therapy
 naproxen: PR, pharmaceuticals
 nonsteroid antiinflammatory agent: AD, drug administration
 nonsteroid antiinflammatory agent: CB, drug combination
 nonsteroid antiinflammatory agent: DT, drug therapy
 nonsteroid antiinflammatory agent: PR, pharmaceuticals
 sodium nitrate: AD, drug administration
 sodium nitrate: DT, drug therapy
 sodium nitrate: PR, pharmaceuticals
 triflupromazine: CB, drug combination
 triflupromazine: DT, drug therapy
 vidarabine: AD, drug administration
 vidarabine: DT, drug therapy
 vidarabine: PR, pharmaceuticals
 vidarabine phosphate: AD, drug administration
 vidarabine phosphate: DT, drug therapy
 vidarabine phosphate: PR, pharmaceuticals
 (aciclovir) 59277-89-3; (amitriptyline) 50-48-6,
 549-18-8; (carbamazepine) 298-46-4, 8047-84-5;
 (idoxuridine) 54-42-2; (lidocaine) 137-58-6, 24847-67-4,
 56934-02-2, 73-78-9; (methylprednisolone sodium succinate)
 2375-03-3, 2921-57-5; (naproxen) 22204-53-1, 26159-34-2;
 (sodium nitrate) 7631-99-4; (triflupromazine) 1098-60-8,
 146-54-3; (vidarabine phosphate) 29984-33-6; (vidarabine)
 2006-02-2, 5536-17-4
 anaprox; elavil; naproxyn; solumedrol; tegretol

CAS REGISTRY NO.:

CHEMICAL NAME:

L91 ANSWER 45 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1996098410 EMBASE Full-text
 TITLE: What's new in pediatric dermatology.
 AUTHOR: Bonifazi, E.
 SOURCE: European Journal of Pediatric Dermatology, (1995) Vol. 5, No. 2, pp. 81-85.
 ISSN: 1122-7672 CODEN: EPDDE9
 COUNTRY: Italy
 DOCUMENT TYPE: Journal; (Short Survey)
 FILE SEGMENT: 013 Dermatology and Venereology

037 Drug Literature Index
 007 Pediatrics and Pediatric Surgery

LANGUAGE: English
 ENTRY DATE: Entered STN: 30 Apr 1996
 Last Updated on STN: 30 Apr 1996

CONTROLLED TERM: Medical Descriptors:
 child
 *cystic fibrosis
 human
 intramuscular drug administration
 intravenous drug administration
 oral drug administration
 *pruritus: DT, drug therapy
 short survey
 *skin disease: CO, complication
 *skin disease: DI, diagnosis
 *skin disease: DT, drug therapy
 *skin disease: ET, etiology
 topical drug administration

CONTROLLED TERM: Drug Descriptors:
 alpha tocopherol: DT, drug therapy
 alprazolam: DT, drug therapy
 amitriptyline: DT, drug therapy
 antibiotic agent: DT, drug therapy
 buspirone: DT, drug therapy
 cimetidine: DT, drug therapy
 clomipramine: DT, drug therapy
 cyclosporin: DT, drug therapy
 dicloxacillin: DT, drug therapy
 diphenhydramine: DT, drug therapy
 doxepin: DT, drug therapy
 fluconazole: DT, drug therapy
 fluoxetine: DT, drug therapy
 haloperidol: DT, drug therapy
 hydroxyzine: DT, drug therapy
 immunoglobulin: DT, drug therapy
 isotretinoin: DT, drug therapy
 ivermectin: DT, drug therapy
 nortriptyline: DT, drug therapy
 penicillin g: DT, drug therapy
 pimozide: DT, drug therapy
 prednisone: DT, drug therapy
 procaine penicillin: DT, drug therapy
 procaine plus lidocaine: DT, drug therapy
 pseudomonic acid: DT, drug therapy
 psychotropic agent: DT, drug therapy
 sertraline: DT, drug therapy
 tetracycline: DT, drug therapy
 unclassified drug

CAS REGISTRY NO.: (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4,
 58-95-7, 59-02-9; (alprazolam) 28981-97-7;
 (amitriptyline) 50-48-6, 549-18-8; (buspirone)
 33386-08-2, 36505-84-7; (cimetidine) 51481-61-9,
 70059-30-2; (clomipramine) 17321-77-6, 303-49-1;
 (cyclosporin) 79217-60-0; (dicloxacillin) 13412-64-1,
 3116-76-5, 343-55-5; (diphenhydramine) 147-24-0, 58-73-1;
 (doxepin) 1229-29-4, 1668-19-5; (fluconazole)
 86386-73-4; (fluoxetine) 54910-89-3, 56296-78-7,
 59333-67-4; (haloperidol) 52-86-8; (hydroxyzine) 2192-20-3,
 64095-02-9, 68-88-2; (immunoglobulin) 9007-83-4;

(isotretinoin) 4759-48-2; (ivermectin) 70288-86-7;
 (nortriptyline) 72-69-5, 894-71-3; (penicillin G)
 1406-05-9, 61-33-6; (pimozide) 2062-78-4; (prednisone)
 53-03-2; (procaine penicillin) 54-35-3, 6130-64-9;
 (pseudomonic acid) 12650-69-0, 40980-51-6, 71980-98-8;
 (sertraline) 79617-96-2; (tetracycline) 23843-90-5,
 60-54-8, 64-75-5
 CHEMICAL NAME: afranil; atarax; benadryl; buspar; elavil; haldol;
 rap; pamelor; prozac; sinequan; xanax; zolof

L91 ANSWER 46 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1994279719 EMBASE Full-text
 TITLE: Benign tumors of the breast.
 AUTHOR: Isaacs, J.H., Dr. (correspondence)
 CORPORATE SOURCE: Department of Obstetrics/Gynecology, Loyola University,
 3008 Indian Wood Road, Wilmette, IL 60091-1130, United States.
 SOURCE: Obstetrics and Gynecology Clinics of North America, (1994)
 Vol. 21, No. 3, pp. 487-497.
 ISSN: 0889-8545 CODEN: OGCAE8
 COUNTRY: United States
 DOCUMENT TYPE: Journal; General Review; (Review)
 FILE SEGMENT: 010 Obstetrics and Gynecology
 003 Endocrinology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 005 General Pathology and Pathological Anatomy

LANGUAGE: English
 SUMMARY LANGUAGE: English

ABSTRACT: Most patients who consult their physician for 'breast lesions' do not have a malignancy of the breast. The benign lesions of the breast include fibrocystic condition, macrocyst fibroadenomas, and intraductal papillomas. Nipple discharge is a common condition, and the diagnosis and treatment is discussed. Rarer benign tumors such as adenoid tumors, lipomas, neurofibromatosis, benign fibrous histiocytoma, and glandular cell tumors are briefly discussed.

CONTROLLED TERM: Medical Descriptors:
 breast abscess: SU, surgery
 breast biopsy
 breast cancer: DI, diagnosis
 *breast cyst: DI, diagnosis
 breast discharge: DI, diagnosis
 breast duct ectasia: DI, diagnosis
 breast duct ectasia: ET, etiology
 breast milk: EC, endogenous compound
 breast papilloma: DI, diagnosis
 breast papilloma: SU, surgery
 *breast tumor: DI, diagnosis
 *breast tumor: DT, drug therapy
 *breast tumor: ET, etiology
 *breast tumor: SU, surgery
 estrogen therapy
 female
 *fibroadenoma: DI, diagnosis
 *fibroadenoma: SU, surgery
 *fibrocystic breast disease: DI, diagnosis
 galactorrhea: CO, complication
 galactorrhea: DI, diagnosis

galactorrhea: DT, drug therapy
galactorrhea: ET, etiology
galactorrhea: SI, side effect
human
mammography
mastalgia: CO, complication
mastalgia: DT, drug therapy
mastalgia: ET, etiology
mastitis: DT, drug therapy
physical examination
priority journal
review
Tietze syndrome: CO, complication
Tietze syndrome: DI, diagnosis
Tietze syndrome: DT, drug therapy
CONTROLLED TERM: Drug Descriptors:
antibiotic agent: DT, drug therapy
antiinflammatory agent: DT, drug therapy
bromocriptine mesilate: DO, drug dose
bromocriptine mesilate: DT, drug therapy
bromocriptine mesilate: PD, pharmacology
estrogen: DT, drug therapy
estrogen: EC, endogenous compound
hexachlorophene
ice
lactose: EC, endogenous compound
methyldopa: AE, adverse drug reaction
nonsteroid antiinflammatory agent: DT, drug therapy
oral contraceptive agent: AE, adverse drug reaction
oral contraceptive agent: AD, drug administration
phenothiazine derivative: AE, adverse drug reaction
povidone iodine
progesterone: DT, drug therapy
prolactin: EC, endogenous compound
Rauwolfia alkaloid: AE, adverse drug reaction
tricyclic antidepressant agent: AE, adverse drug reaction
CAS REGISTRY NO.: (bromocriptine mesilate) 22260-51-1; (hexachlorophene) 11119-93-0, 70-30-4; (lactose) 10039-26-6, 16984-38-6, 63-42-3, 64044-51-5; (methyldopa) 555-29-3, 555-30-6; (povidone iodine) 25655-41-8; (progesterone) 57-83-0; (prolactin) 12585-34-1, 50647-00-2, 9002-62-4
CHEMICAL NAME: parlodel
L91 ANSWER 47 OF 49 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1992160861 EMBASE Full-text
TITLE: Bayesian parameter estimation and population pharmacokinetics.
AUTHOR: Thomson, A.H., Dr. (correspondence); Whiting, B.
CORPORATE SOURCE: Dept of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT, United Kingdom.
SOURCE: Clinical Pharmacokinetics, (1992) Vol. 22, No. 6, pp. 447-467.
ISSN: 0312-5963 CODEN: CPKNDH
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

10/524815

ENTRY DATE: Entered STN: 21 Jun 1992
Last Updated on STN: 21 Jun 1992

ABSTRACT: The widespread application of Bayesian parameter estimation in the area of therapeutic drug monitoring (TDM) has prompted the need for well conducted population studies to obtain relevant prior pharmacokinetic parameter estimates. In many cases the population has consisted of a relatively small number of subjects. This may be unavoidable for drugs used in cancer chemotherapy or in small, specific populations of patients. In contrast, information about drugs which are used extensively, such as the aminoglycosides, can be obtained by population studies which involve a large number of individuals. Indeed, this technique has proved particularly useful for determining parameter estimates which can be employed in neonatal TDM. Bayesian parameter estimation has been most frequently used for drugs with narrow therapeutic ranges such as the aminoglycosides, cyclosporin, digoxin, anticonvulsants (especially phenytoin), lithium and theophylline. However, the technique has now been extended to cytotoxic drugs, Factor VIII and warfarin. Bayesian methods have also been used to limit the number of samples required in more conventional pharmacokinetic studies with new drugs. Further advances in the use of these methods are likely to include measures of drug response and toxicity requiring population studies which also include relevant pharmacodynamic information.

CONTROLLED TERM: Medical Descriptors:
*bayes theorem
cancer chemotherapy
cystic fibrosis
drug blood level
drug monitoring
drug response
drug urine level
forecasting
neonatology
*pharmacokinetics
*population research
priority journal
review
sample
toxicity

CONTROLLED TERM: Drug Descriptors:
alfentanil: PK, pharmacokinetics
aminoglycoside: PK, pharmacokinetics
anticonvulsive agent: PK, pharmacokinetics
bentazepam: PK, pharmacokinetics
blood clotting factor 8: PK, pharmacokinetics
ceftazidime: PK, pharmacokinetics
ciprofloxacin: PK, pharmacokinetics
cyclosporin: PK, pharmacokinetics
cytotoxic agent: PK, pharmacokinetics
digoxin: PK, pharmacokinetics
heparin: PK, pharmacokinetics
imipramine: PK, pharmacokinetics
lidocaine: PK, pharmacokinetics
lithium: PK, pharmacokinetics
midazolam: PK, pharmacokinetics
piperacillin: PK, pharmacokinetics
theophylline: PK, pharmacokinetics
vancomycin: PK, pharmacokinetics
warfarin: PK, pharmacokinetics

CAS REGISTRY NO.: (alfentanil) 69049-06-5, 71195-58-9; (bentazepam)
29462-18-8; (blood clotting factor 8) 9001-27-8;

(ceftazidime) 72558-82-8; (ciprofloxacin) 85721-33-1;
 (cyclosporin) 79217-60-0; (digoxin) 20830-75-5, 57285-89-9;
 (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5;
 (imipramine) 113-52-0, 50-49-7; (lidocaine) 137-58-6,
 24847-67-4, 56934-02-2, 73-78-9; (lithium) 7439-93-2;
 (midazolam) 59467-70-8; (piperacillin) 59703-84-3,
 61477-96-1; (theophylline) 58-55-9, 5967-84-0, 8055-07-0,
 8061-56-1, 99007-19-9; (vancomycin) 1404-90-6, 1404-93-9;
 (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8,
 81-81-2

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ACCESSION NUMBER: 1991065459 EMBASE Full-text
 TITLE: Chronic bronchial secretion in Δ F508 heterozygote for cystic fibrosis.
 AUTHOR: Smith, D.L.; Stableforth, D.E.; Cushley, M.
 CORPORATE SOURCE: Adult Cystic Fibrosis Unit, East Birmingham Hospital, Birmingham B9 5ST, United Kingdom.
 SOURCE: Lancet, (1991) Vol. 337, No. 8735, pp. 234.
 ISSN: 0140-6736 CODEN: LANCAO
 COUNTRY: United Kingdom
 DOCUMENT TYPE: Journal; Letter
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 022 Human Genetics
 030 Clinical and Experimental Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 ENTRY DATE: Entered STN: 16 Dec 1991
 Last Updated on STN: 16 Dec 1991
 CONTROLLED TERM: Medical Descriptors:
 adult
 case report
 *cystic fibrosis: DI, diagnosis
 *cystic fibrosis: DT, drug therapy
 *genetic analysis
 *heterozygote
 human
 letter
 male
 priority journal
 CONTROLLED TERM: Drug Descriptors:
 *antihistaminic agent
 *cholinergic receptor blocking agent
 *corticosteroid
 *tricyclic antidepressant agent

L91 ANSWER 49 OF 49 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 1968:78186 BIOSIS Full-text
 DOCUMENT NUMBER: PREV19684900078189; BA49:78189
 TITLE: letter asthmatic woman.
 Original Title: Amitriptyline and sputum viscosity.
 AUTHOR(S): BAILLIE, RITA M.
 CORPORATE SOURCE: Monyhull Hosp., Birmingham, Engl., UK
 SOURCE: LANCET, (1967) Vol. 2, No. 7511, pp. 369-370.
 DOCUMENT TYPE: Article
 FILE SEGMENT: BA
 LANGUAGE: Unavailable
 ENTRY DATE: Entered STN: May 2007

Last Updated on STN: May 2007

ABSTRACT: An asthmatic woman had increased sputum viscosity when given 150 mg amitriptyline daily for depression. When the dosage was halved, the sputum became more fluid. A 16 year old girl with fibrocystic disease of the pancreas and associated chronic chest infection given amitriptyline, had the same results.

CONCEPT CODE: Pharmacology - Immunological processes and allergy 22018
INDEX TERMS: Major Concepts
Pharmacology
INDEX TERMS: Parts, Structures, & Systems of Organisms
pancreas: digestive system, endocrine system; sputum
INDEX TERMS: Diseases
chronic chest infection: disease, Infection
INDEX TERMS: Diseases
infection: infectious disease
Infection (MeSH)
INDEX TERMS: Chemicals & Biochemicals
amitriptyline
REGISTRY NUMBER: 50-48-6 (amitriptyline)

=> file registry

FILE 'REGISTRY' ENTERED AT 11:28:47 ON 14 OCT 2009
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DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

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FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCaplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate
substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

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L25      609 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR
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L26      155 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI
L27      5892 SEA FILE=ZCAPLUS SPE=ON ABB=ON PLU=ON CFTR/BI
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          L27 OR L28)
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          TETRACYCLIC?/BI) AND L29
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          OR BAC OR PKT OR PAC)/RL) AND L63

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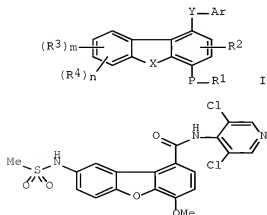
L74 ANSWER 1 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:99226 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:197859
TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,
9H-carbazole-4-carboxamides, and
dibenzo[b,d]thiophene-4-carboxamides as PDE4
inhibitors for the treatment of inflammatory and

```

INVENTOR(S): allergic disorders
 Gopalan, Balasubramanian; Gharat, Laxmikant A.;
 Lakdawala, Aftab D.; Karunakaran, Usha
 PATENT ASSIGNEE(S): Glenmark Pharmaceuticals, Inc. USA, USA
 SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of Appl.
 No. PCT/IB04/000355.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050027129	A1	20050203	US 2004-821642	20040409 <--
US 7223789	B2	20070529		
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411 <--
WO 2004089940	A1	20041021	WO 2004-IB355	20040211 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ZA 2005008240	A	20060531	ZA 2005-8240	20051012 <--
US 20070105854	A1	20070510	US 2006-536434	20060928 <--
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928 <--
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602 <--
PRIORITY APPLN. INFO.:				
			IN 2003-MU363	A 20030411 <--
			US 2003-519967P	P 20031113 <--
			WO 2004-IB355	A2 20040211
			US 2004-821642	A3 20040409
			US 2006-536434	A1 20060928

OTHER SOURCE(S): MARPAT 142:197859
 GI



II

- AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6 (R5, R6 = H, alkyl, cycloalkyl, etc.), heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SOO-2, NRa; Y = CONR7, NR7SOO-2, SOO-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; Ra = H, alkyl, cycloalkyl, etc.; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenzo[b,f]furan-1- carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D333-76
ICS C07D209-82; C07D307-91
- INCL 549048000; 548444000; 549460000
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;
tricyclic heterocycle prepn phosphodiesterase 4 inhibitor
antiinflammatory antiallergic antidiabetic
- IT Inflammation
(Crohn's disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
(Crohn's, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Inflammation
Nose, disease
(allergic rhinitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
(allergic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis
(atopic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease
(cerebrovascular, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and

- inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease
 - Inflammation
 - (chronic bronchitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease
 - (chronic obstructive pulmonary disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - (chronic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (dementia, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (depression, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma
 - (eosinophilic, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease
 - (failure, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - (inflammation, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
- Heart, disease
- Intestine, disease
- Joint, anatomical
- Lung, disease
- Skin, disease
 - (inflammatory conditions or immune disorders, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
 - (inflammatory, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus
 - (insulin-resistant, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
- Kidney, disease
 - (nephritis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
- Alzheimer's disease
- Anti-Alzheimer's agents
- Anti-inflammatory agents

- Antiarthritics
- Antiasthmatics
- Antidepressants
- Antidiabetic agents
- Antirheumatic agents
- Cardiovascular agents
- Drug delivery systems
- Human
- Immunomodulators
- Nervous system agents
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tricyclic compounds
 - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
 - (rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - Spinal column, disease
 - (spondylitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
- Cystic fibrosis
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Urticaria
 - (treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - Intestine, disease
 - (ulcerative colitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
 - Inflammation
 - (uveitis; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
- 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-

acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)

IT 778576-35-5P 778576-36-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
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 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(3-
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 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
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 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide

hydrochloride 778576-56-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[4-(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(morpholin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P,
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 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-73-1P, N-Phenyl-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-83-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P
 778576-88-8P 778576-89-9P,
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-carboxamide 778576-95-7P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-96-8P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-99-1P 778577-06-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778581-69-4P

RL: FAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

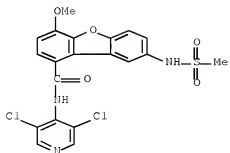
- IT 2973-58-2P, 2-Bromoisoanillin 19688-46-1P, 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P, 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P, 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P, 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P, 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P, 4-Cyclopentyl-3-hydroxybenzaldehyde 685873-89-6P, 2-Bromo-4-cyclopentyl-3-hydroxybenzaldehyde 685873-90-9P, 2-Bromo-4-cyclopentyl-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P, 4-Cyclopentyl-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P, 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P, 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P, 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P, N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-carboxamide 778576-29-7P, Methyl 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P, 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P, N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P 778577-04-1P 778577-05-2P
- RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
- (intermediate; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 9036-21-9, Phosphodiesterase type 4
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 836627-26-0P
- RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9,

4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7,
 N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9,
 Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9,
 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5,
 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl
 isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin
 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8,
 Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8,
 Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride
 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6,
 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7,
 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl
 3-amino-4-methoxybenzoate 778576-75-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of tricyclic heterocycles as PDE4 inhibitors for
 treatment of immune and inflammatory disorders and insulin resistant
 diabetes)

IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-(n-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)

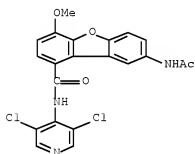
RN 778576-34-4 ZCAPLUS
 CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-
 [(methylsulfonyl)amino]- (CA INDEX NAME)

10/524815



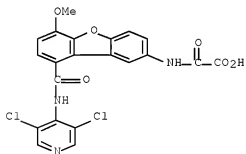
RN 778576-37-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-41-3 ZCAPLUS

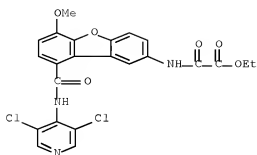
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



RN 778576-42-4 ZCAPLUS

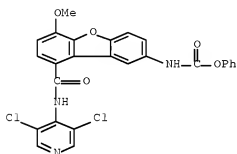
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)

10/524815



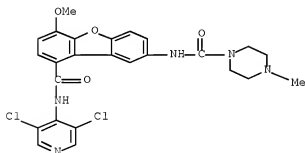
RN 778576-49-1 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, phenyl ester (9CI) (CA INDEX NAME)



RN 778576-54-8 ZCAPLUS

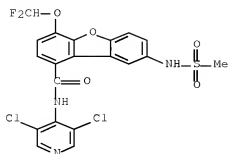
CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl- (CA INDEX NAME)



RN 778576-62-8 ZCAPLUS

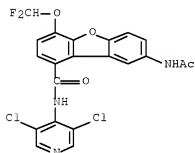
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)

10/524815



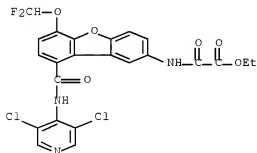
RN 778576-66-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-69-5 ZCAPLUS

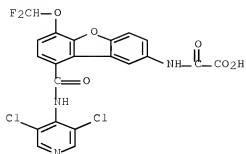
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



RN 778576-70-8 ZCAPLUS

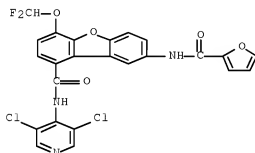
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)

10/524815



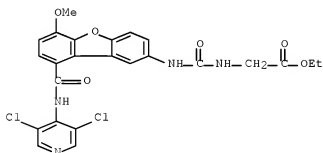
RN 778576-72-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]- (CA INDEX NAME)



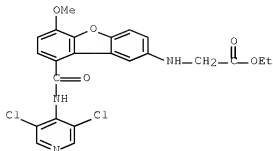
RN 778576-90-2 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]-, ethyl ester (CA INDEX NAME)



RN 778576-92-4 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (CA INDEX NAME)



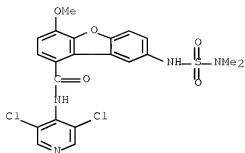
IT 778576-35-5P 778576-36-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(3-
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(furan-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-46-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isobutyloxy)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 hydrochloride 778576-56-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(4-hydroxypiperidin-1-
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(morpholin-4-
 yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-60-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-61-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-

[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778576-64-QP, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
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 778576-65-1P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium
 salt 778576-73-1P, N-Phenyl-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,
 N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-80-QP, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-
 carboxamide 778576-83-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P
 778576-88-8P 778576-89-9P,
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-
 hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-
 2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-
 carboxamide 778576-95-7P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-96-8P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-97-9P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-
 carbazole-4-carboxamide 778576-98-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt
 778576-99-1P 778577-06-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide sodium salt
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778581-69-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)

RN 778576-35-5 ZCAPLUS

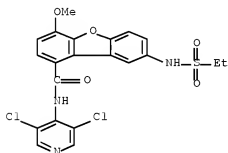
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
 [[(dimethylamino)sulfonyl]amino]-4-methoxy- (CA INDEX NAME)

10/524815



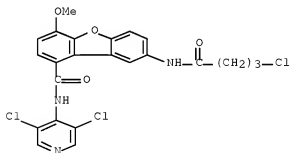
RN 778576-36-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
[(ethylsulfonyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-38-8 ZCAPLUS

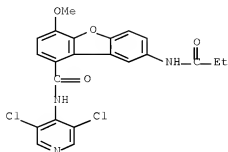
CN 1-Dibenzofurancarboxamide, 8-[(4-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-
4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-39-9 ZCAPLUS

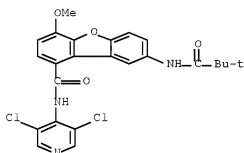
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(1-
oxopropyl)amino]- (CA INDEX NAME)

10/524815



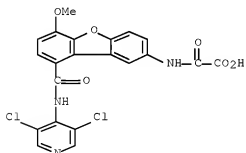
RN 778576-40-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2,2-dimethyl-1-oxopropyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-43-5 ZCAPLUS

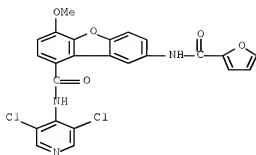
CN Acetic acid, 2-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:1) (CA INDEX NAME)



● Na

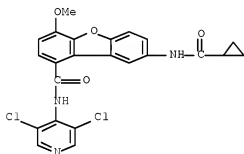
RN 778576-44-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2-furanylcarbonyl)amino]-4-methoxy- (CA INDEX NAME)



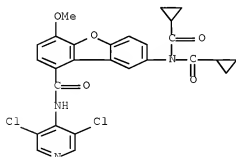
RN 778576-45-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



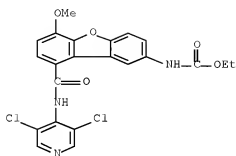
RN 778576-46-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[bis(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



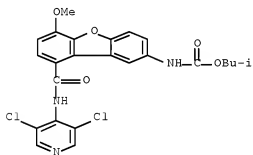
RN 778576-47-9 ZCAPLUS

CN Carbamic acid, [9-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl-, ethyl ester (9CI) (CA INDEX NAME)



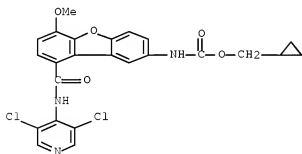
RN 778576-48-0 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



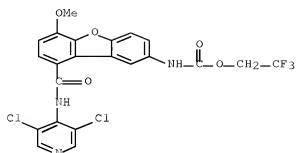
RN 778576-50-4 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)



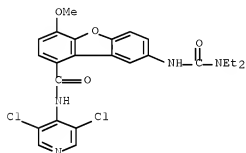
RN 778576-51-5 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2,2,2-trifluoroethyl ester (9CI) (CA INDEX NAME)



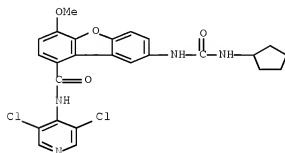
RN 778576-52-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[diethylamino]carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-53-7 ZCAPLUS

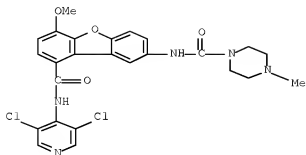
CN 1-Dibenzofurancarboxamide, 8-[(cyclopentylamino)carbonyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-55-9 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl-, hydrochloride (1:1) (CA INDEX NAME)

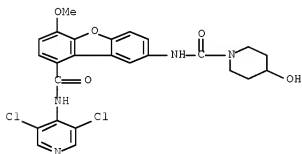
10/524815



● HCl

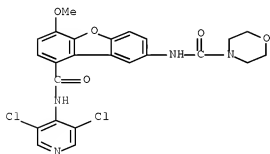
RN 778576-56-0 ZCAPLUS

CN 1-Piperidinecarboxamide, N-[9-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-hydroxy- (CA INDEX NAME)



RN 778576-57-1 ZCAPLUS

CN 4-Morpholinecarboxamide, N-[9-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)

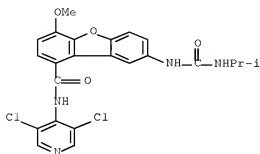


RN 778576-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[[1-

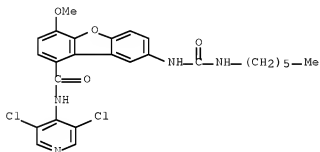
10/524815

methylethyl)amino]carbonyl]amino]- (CA INDEX NAME)



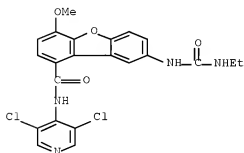
RN 778576-59-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
[[hexylamino]carbonyl]amino]-4-methoxy- (CA INDEX NAME)



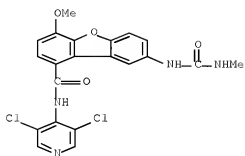
RN 778576-60-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
[[ethylamino]carbonyl]amino]-4-methoxy- (CA INDEX NAME)



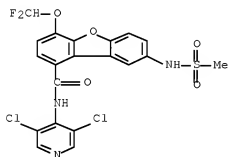
RN 778576-61-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-
[[methylamino]carbonyl]amino]- (CA INDEX NAME)



RN 778576-63-9 ZCAPLUS

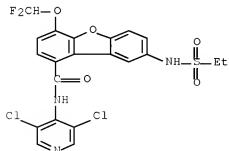
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)



● Na

RN 778576-64-0 ZCAPLUS

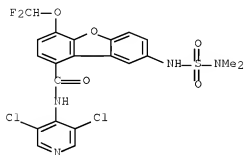
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(ethylsulfonyl)amino]- (CA INDEX NAME)



10/524815

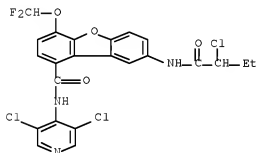
RN 778576-65-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[[(dimethylamino)sulfonyl]amino]- (CA INDEX NAME)



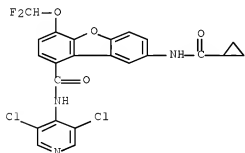
RN 778576-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(2-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-68-4 ZCAPLUS

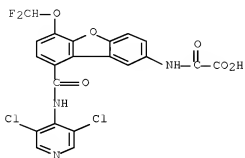
CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-71-9 ZCAPLUS

10/524815

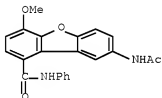
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

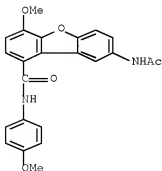
RN 778576-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-phenyl- (CA INDEX NAME)



RN 778576-77-5 ZCAPLUS

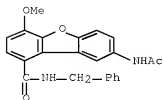
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



10/524815

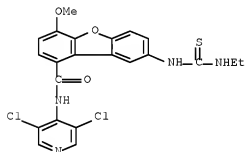
RN 778576-80-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)-
(CA INDEX NAME)



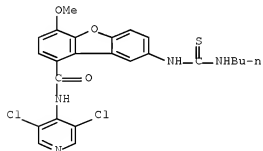
RN 778576-83-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
[[ethylamino]thioxomethylamino]-4-methoxy- (CA INDEX NAME)



RN 778576-84-4 ZCAPLUS

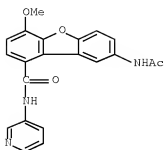
CN 1-Dibenzofurancarboxamide, 8-[[butylamino]thioxomethylamino]-N-(3,5-
dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-85-5 ZCAPLUS

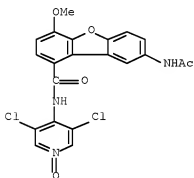
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-3-pyridinyl- (CA
INDEX NAME)

10/524815



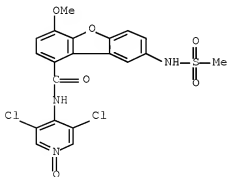
RN 778576-87-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-88-8 ZCAPLUS

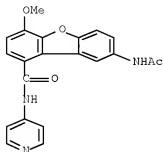
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



RN 778576-89-9 ZCAPLUS

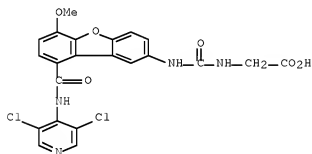
10/524815

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-4-pyridinyl- (CA
INDEX NAME)



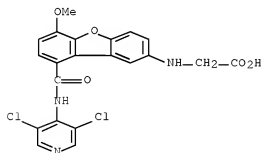
RN 778576-91-3 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]- (CA INDEX NAME)



RN 778576-93-5 ZCAPLUS

CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)

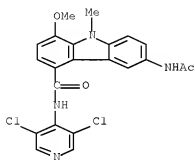


RN 778576-94-6 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-1-

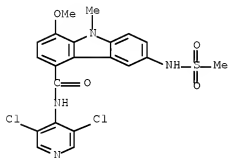
10/524815

methoxy-9-methyl- (CA INDEX NAME)



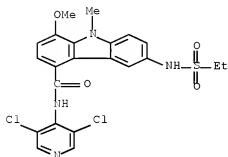
RN 778576-95-7 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]- (CA INDEX NAME)



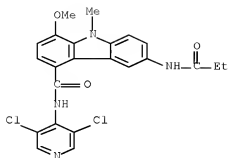
RN 778576-96-8 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-6-[(ethylsulfonyl)amino]-1-methoxy-9-methyl- (CA INDEX NAME)



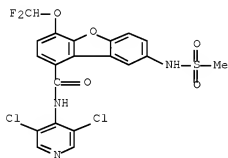
RN 778576-97-9 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(1-oxopropyl)amino]- (CA INDEX NAME)



RN 778576-98-0 ZCAPLUS

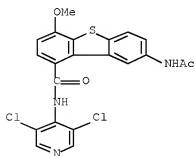
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

RN 778576-99-1 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-, sodium salt (1:2) (CA INDEX NAME)

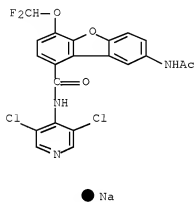


●2 Na

10/524815

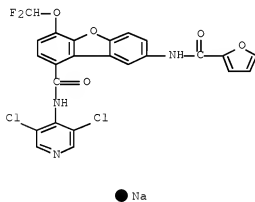
RN 778577-06-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-, sodium salt (1:1) (CA INDEX NAME)



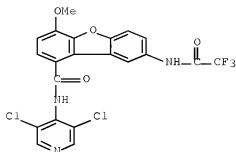
RN 778577-07-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)



RN 778581-69-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(2,2,2-trifluoroacetyl)amino]- (CA INDEX NAME)



IT 836627-26-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

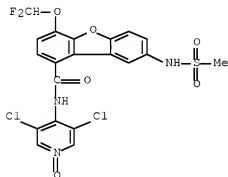
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)

RN 836627-26-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 2 OF 7 ZCAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2004:1127375 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 142:74464

TITLE: Preparation of tricyclic compounds useful for the treatment of inflammatory and allergic disorders
 INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

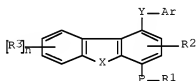
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
 SOURCE: PCT Int. Appl., 55 pp.

DOCUMENT TYPE: Patent
 LANGUAGE: English

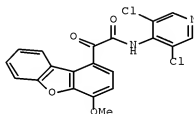
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111044	A1	20041223	WO 2004-IB1643	20040616 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00631	A	20050211	IN 2003-MU631	20030617 <--
PRIORITY APPLN. INFO.:			IN 2003-MU631	A 20030617 <--
OTHER SOURCE(S):		MARPAT 142:74464		
GI				



I



II

- AB The title compds. I [R1-R3 = H, alkyl, cycloalkyl, aryl, etc.; n = 0-4; X = O, S(O)m, NRA (wherein m = 0-2; Ra = H, alkyl, cycloalkyl, etc.); P = O, S; Ar = (un)substituted aryl, arylalkyl, heterocyclyl, heteroaryl; Y = C(A)C(B)NR4 (wherein A, B = O, S, NRA; R4 = H, alkyl, OH, aryl, etc.)] which are novel phosphodiesterase type 4 (PDE4) inhibitors useful for the treatment of inflammatory and allergic disorders, were prepared Thus, reacting 2-(4-methoxydibenzo[b,f]furan-1-yl)-2-oxoacetic acid (preparation given) with 4-amino-3,5-dichloropyridine afforded II which showed IC50 of 184 nM against PDE4.
- IC ICM C07D405-12
ICS A61K031-343
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- ST tricyclic compd prepn phosphodiesterase 4 PDE4 inhibitor
antiinflammatory; dibenzofuranyloxoacetamide prepn phosphodiesterase 4 PDE4 inhibitor antiinflammatory allergy asthma
- IT Allergy
Alzheimer's disease
Amnesia
Asthma
Central nervous system, disease
Cystic fibrosis

Eczema
 Gout
 Immune disease
 Inflammation
 Multiple sclerosis
 Osteoarthritis
 Psoriasis
 Rheumatoid arthritis
 Shock (circulatory collapse)
 Urticaria

(treating; preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors

for

the treatment of inflammatory and allergic disorders)

IT	815586-07-3P	815586-08-4P	815586-09-5P
	815586-10-8P	815586-11-9P	815586-12-0P
	815586-13-1P	815586-14-2P	815586-15-3P
	815586-16-4P	815586-17-5P	815586-18-6P
	815586-19-7P		

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the treatment of inflammatory and allergic disorders)

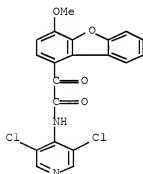
IT	815586-07-3P	815586-08-4P	815586-09-5P
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	815586-16-4P	815586-17-5P	815586-18-6P
	815586-19-7P		

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

(preparation of dibenzofuranyloxoacetamides as PDE4 inhibitors for the treatment of inflammatory and allergic disorders)

RN 815586-07-3 ZCAPLUS

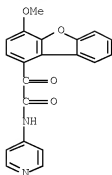
CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- α -
 oxo- (CA INDEX NAME)



RN 815586-08-4 ZCAPLUS

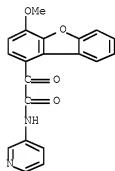
CN 1-Dibenzofuranacetamide, 4-methoxy- α -oxo-N-4-pyridinyl- (CA INDEX
 NAME)

10/524815



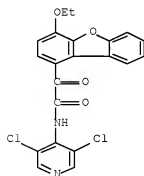
RN 815586-09-5 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-methoxy- α -oxo-N-3-pyridinyl- (CA INDEX NAME)



RN 815586-10-8 ZCAPLUS

CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-ethoxy- α -oxo- (CA INDEX NAME)

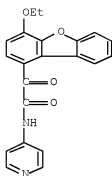


RN 815586-11-9 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-ethoxy- α -oxo-N-4-pyridinyl- (CA INDEX NAME)

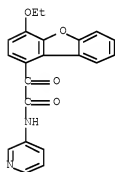
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(NAME)



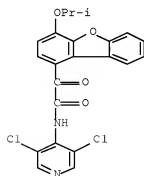
RN 815586-12-0 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-ethoxy- α -oxo-N-3-pyridinyl- (CA INDEX NAME)



RN 815586-13-1 ZCAPLUS

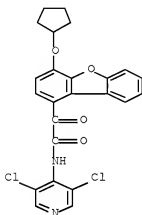
CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-(1-methylethoxy)- α -oxo- (CA INDEX NAME)



10/524815

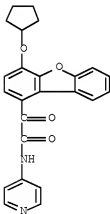
RN 815586-14-2 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)- α -oxo- (CA INDEX NAME)



RN 815586-15-3 ZCAPLUS

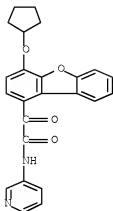
CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)- α -oxo-N-4-pyridinyl- (CA INDEX NAME)



RN 815586-16-4 ZCAPLUS

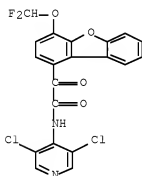
CN 1-Dibenzofuranacetamide, 4-(cyclopentyloxy)- α -oxo-N-3-pyridinyl- (CA INDEX NAME)

10/524815



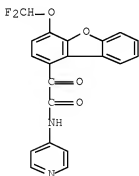
RN 815586-17-5 ZCAPLUS

CN 1-Dibenzofuranacetamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-
 α -oxo- (CA INDEX NAME)



RN 815586-18-6 ZCAPLUS

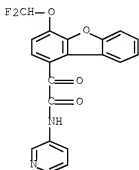
CN 1-Dibenzofuranacetamide, 4-(difluoromethoxy)- α -oxo-N-4-pyridinyl-
 (CA INDEX NAME)



10/524815

RN 815586-19-7 ZCAPLUS

CN 1-Dibenzofuranacetamide, 4-(difluoromethoxy)- α -oxo-N-3-pyridinyl-
(CA INDEX NAME)



OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD
(1 CITINGS)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 3 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:878393 ZCAPLUS Full-text

DOCUMENT NUMBER: 141:366121

TITLE: Preparation of dibenzo[b,f]furan-1-carboxamides,
9H-carbazole-4-carboxamides, and
dibenzo[b,d]thiophene-4-carboxamides as PDE4
inhibitors for the treatment of inflammatory and
allergic disorders

INVENTOR(S): Gopalan, Balasubramanian; Gharat, Laxmikant Atmaram;
Lakdawala, Aftab Dawoodbhai; Karaunakaran, Usha

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 121 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089940	A1	20041021	WO 2004-IB355	20040211 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00363	A	20050304	IN 2003-MU363	20030411 <--
AU 2004228453	A1	20041021	AU 2004-228453	20040211 <--

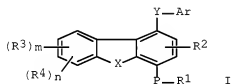
CA 2522023	A1	20041021	CA 2004-2522023	20040211 <--
EP 1620429	A1	20060201	EP 2004-710093	20040211 <--
EP 1620429	B1	20090401		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004009747	A	20060509	BR 2004-9747	20040211 <--
CN 1829711	A	20060906	CN 2004-80016048	20040211 <--
JP 2006522789	T	20061005	JP 2006-506259	20040211 <--
NZ 542882	A	20071026	NZ 2004-542882	20040211 <--
AT 427308	T	20090415	AT 2004-710093	20040211 <--
ES 2320888	T3	20090529	ES 2004-710093	20040211 <--
AP 2008	A	20090630	AP 2005-3424	20040211 <--
US 20050027129	A1	20050203	US 2004-821642	20040409 <--
US 7223789	B2	20070529		
MX 2005010948	A	20060531	MX 2005-10948	20051011 <--
ZA 2005008240	A	20060531	ZA 2005-8240	20051012 <--
NO 2005005316	A	20060111	NO 2005-5316	20051110 <--
US 20070105854	A1	20070510	US 2006-536434	20060928 <--
US 7384962	B2	20080610		
US 20070105855	A1	20070510	US 2006-536448	20060928 <--
US 7393846	B2	20080701		
US 20090182143	A1	20090716	US 2008-131286	20080602 <--

PRIORITY APPLN. INFO.:

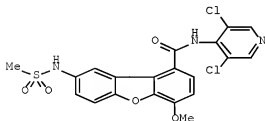
IN 2003-MU363	A	20030411 <--
US 2003-519967P	P	20031113 <--
WO 2004-IB355	W	20040211
US 2004-821642	A3	20040409
US 2006-536434	A1	20060928

OTHER SOURCE(S): CASREACT 141:366121; MARPAT 141:366121

GI



I



II

AB Title heterocyclic tricycles I [wherein R1-R3, R5, R6, Ra = independently H, (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, (hetero)aryl, heterocyclyl(alkyl), etc.; R4 = NR5R6, heterocyclyl; Ar = (un)substituted aryl(alkyl), heterocyclyl, heteroaryl; X = O, SO0-2, NRa; Y = CONR7, NR7SO0-2, SO0-2NR7, NR7CO; R7 = H, OH, ORa, (un)substituted alkyl, aryl, heterocyclyl; P = O, S; m = 0-3; n = 1-4; and tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, N-oxides, pharmaceutically acceptable

- salts, solvates, and compns. thereof] were prepared as phosphodiesterase type 4 (PDE4) inhibitors. For example, N-(3,5-dichloropyrid-4-yl)-4-methoxy-8-aminodibenz[b,f]furan-1-carboxamide (prepared in six steps from isovanillin, 4-fluoronitrobenzene, and 4-amino-3,5-dichloropyridine) was coupled with methanesulfonyl chloride in THF and pyridine to give the sulfonamide II. The latter inhibited the PDE4-induced conversion of [3H] cAMP to the corresponding [3H] 5'-AMP with IC50 of 0.5058 nM. Thus, I and their pharmaceutical compns. are useful for the treatment of immune disorders, inflammatory conditions, allergic conditions, CNS diseases, and insulin resistant diabetes (no data).
- IC ICM C07D405-12
ICS C07D405-14; C07D307-91; C07D401-12; C07D409-12; A61K031-4427; A61P029-00
- CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
- ST dibenzofurancarboxamide carbazolecarboxamide dibenzothiophenecarboxamide
prepn PDE4 inhibitor antiinflammatory antiallergic antidiabetic;
tricyclic heterocycle prepn phosphodiesterase 4 inhibitor
antiinflammatory antiallergic antidiabetic
- IT Inflammation
(Crohn's disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
(Crohn's, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Eye, disease
Inflammation
(allergic conjunctivitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
Inflammation
Nose, disease
(allergic rhinitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
(allergic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Dermatitis
(atopic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Brain, disease
(cerebrovascular, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Bronchi, disease
Inflammation
(chronic bronchitis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and

- inflammatory disorders and insulin resistant diabetes)
- IT Lung, disease
 - (chronic obstructive pulmonary disease, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
 - (chronic, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Anti-inflammatory agents
 - (chronic; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (dementia, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Mental and behavioral disorders
 - (depression, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Granuloma
 - (eosinophilic, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Heart, disease
 - (failure, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
 - (inflammation, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eye, disease
- Heart, disease
- Intestine, disease
- Joint, anatomical
- Lung, disease
- Skin, disease
 - (inflammatory conditions or immune disorders, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Intestine, disease
 - (inflammatory, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Diabetes mellitus
 - (insulin-resistant, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
- Kidney, disease
 - (nephritis, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy inhibitors
 - Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Antiarthritics
 - Antiasthmatics

- Antidepressants
- Antidiabetic agents
- Antirheumatic agents
- Cardiovascular agents
- Drug delivery systems
- Human
- Immunomodulators
- Nervous system agents
- Polymorphism (crystal)
 - (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tumor necrosis factors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Tricyclic compounds
 - RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Eczema
- Gout
- Osteoarthritis
 - (rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
- Spinal column, disease
 - (spondylitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Allergy
- Amnesia
- Asthma
- Central nervous system, disease
- Cystic fibrosis
- Immune disease
- Inflammation
- Multiple sclerosis
- Psoriasis
- Respiratory distress syndrome
- Rheumatoid arthritis
- Shock (circulatory collapse)
- Urticaria
 - (treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT Inflammation
- Intestine, disease
 - (ulcerative colitis, rheumatoid, treatment of; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
- 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,

N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-70-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(2-
 ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)
 IT 778576-35-5P 778576-36-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[[(3-
 chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-
 butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium
 salt 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-46-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(isobutyl)oxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-
 methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 hydrochloride 778576-56-0P,

N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(morpholin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-60-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-61-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-65-1P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P, N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-83-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P, 778576-88-8P, 778576-89-9P, N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(2-hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-carboxamide 778576-95-7P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[[(methylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-96-8P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[[(ethylsulfonyl)amino]-9H-carbazole-4-carboxamide 778576-97-9P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-carbazole-4-carboxamide 778576-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt 778576-99-1P, 778577-06-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide sodium salt 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-[[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt 778581-69-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)

- (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 2973-58-2P, 2-Bromoisoavanillin 19688-46-1P,
 3-Nitro-4-[(2-methoxyphenyl)thio]acetophenone 19688-56-3P,
 3-Amino-4-[(2-methoxyphenyl)thio]acetophenone 685873-72-7P,
 2-Bromo-3-(p-nitrophenoxy)-4-methoxybenzaldehyde 685873-73-8P,
 4-Methoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-74-9P,
 4-Methoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685873-88-5P,
 4-Cyclopentyl-3-hydroxybenzaldehyde 685873-89-6P,
 2-Bromo-4-cyclopentyl-3-hydroxybenzaldehyde 685873-90-9P,
 2-Bromo-4-cyclopentyl-3-(p-nitrophenoxy)benzaldehyde 685873-91-0P,
 4-Cyclopentyl-8-nitro-1-formyldibenzo[b,d]furan 685873-92-1P,
 4-Hydroxy-8-nitro-1-formyldibenzo[b,d]furan 685873-93-2P,
 4-Difluoromethoxy-8-nitro-1-formyldibenzo[b,d]furan 685873-94-3P,
 4-Difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxylic acid 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-81-1P,
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 685875-02-9P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 685875-03-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-28-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-amino-9H-carbazole-4-carboxamide 778576-29-7P, Methyl 3-(2-bromo-4-nitroanilino)-4-methoxybenzoate 778576-30-0P, Methyl 1-methoxy-6-nitro-9H-carbazole-4-carboxylate 778576-31-1P, Methyl 1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylate 778576-32-2P, 1-Methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxylic acid 778576-33-3P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-nitro-9H-carbazole-4-carboxamide 778576-74-2P, N-Phenyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-76-4P, N-Phenyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-78-6P, N-(4-Methoxyphenyl)-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-79-7P, N-(4-Methoxyphenyl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-81-1P, N-Benzyl-4-methoxy-8-nitrodibenzo[b,d]furan-1-carboxamide 778576-82-2P, N-Benzyl-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778576-86-6P, N-(Pyridin-3-yl)-4-methoxy-8-aminodibenzo[b,d]furan-1-carboxamide 778577-00-7P 778577-01-8P 778577-02-9P 778577-03-0P 778577-04-1P 778577-05-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 9036-21-9, Phosphodiesterase type 4 9040-59-9, Phosphodiesterase 1 9068-52-4, Phosphodiesterase type 5
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (preparation of tricyclic heterocycles as PDE4 inhibitors for treatment of immune and inflammatory disorders and insulin resistant diabetes)
- IT 62-53-3, Aniline, reactions 79-03-8, Propionyl chloride 104-94-9, 4-Methoxyaniline 109-01-3, n-Methylpiperazine 109-89-7, N,N-Diethylamine, reactions 111-26-2, 1-Hexylamine 137-43-9, Cyclopentyl bromide 139-85-5, 3,4-Dihydroxybenzaldehyde 350-46-9, 4-Fluoronitrobenzene 400-93-1 462-08-8, 3-Aminopyridine 527-69-5, 2-Furancarboxyl chloride 541-41-3, Ethyl chloroformate 542-85-8, Ethyl isothiocyanate 543-27-1, Isobutyl chloroformate 621-59-0, Isovanillin 623-33-6 701-45-1, 3-Bromo-4-fluoronitrobenzene 924-44-7 1003-03-8,

Cyclopentylamine 1885-14-9, Phenyl chloroformate 2516-33-8,
 Cyclopropylmethanol 3282-30-2 4023-34-1, Cyclopropanecarbonyl chloride
 4635-59-0 4755-77-5 5382-16-1, 4-Hydroxypiperidine 7217-59-6,
 2-Methoxybenzenethiol 7623-11-2, 2-Chlorobutanoyl chloride 22889-78-7,
 4-Amino-3,5-dichloropyridine 24812-90-6, Methyl
 3-amino-4-methoxybenzoate 778576-75-3

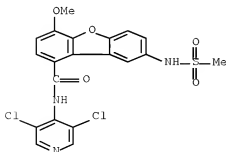
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of tricyclic heterocycles as PDE4 inhibitors for
 treatment of immune and inflammatory disorders and insulin resistant
 diabetes)

IT 778576-34-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-37-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-41-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-49-1P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(phenoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-54-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[
 (N-methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-62-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-69-5P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethoxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-70-8P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-72-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-90-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[
 (2-ethoxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-92-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-ethoxy-2-
 oxoethylamino)dibenzo[b,d]furan-1-carboxamide
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)

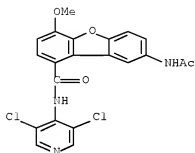
RN 778576-34-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-
 [(methylsulfonyl)amino]- (CA INDEX NAME)



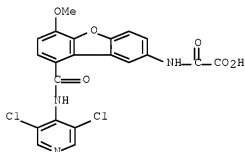
RN 778576-37-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



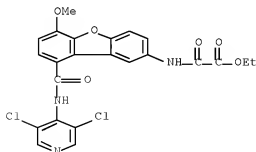
RN 778576-41-3 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



RN 778576-42-4 ZCAPLUS

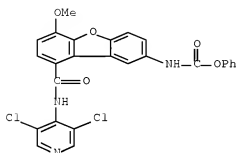
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



10/524815

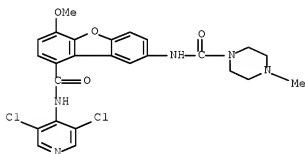
RN 778576-49-1 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, phenyl ester (9CI) (CA INDEX NAME)



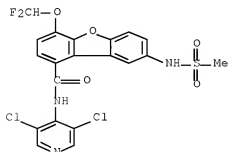
RN 778576-54-8 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl- (CA INDEX NAME)



RN 778576-62-8 ZCAPLUS

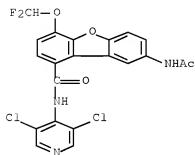
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



10/524815

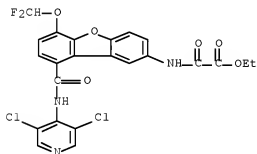
RN 778576-66-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



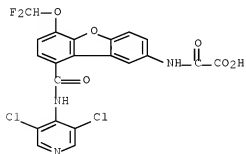
RN 778576-69-5 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, ethyl ester (CA INDEX NAME)



RN 778576-70-8 ZCAPLUS

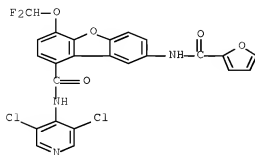
CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo- (CA INDEX NAME)



10/524815

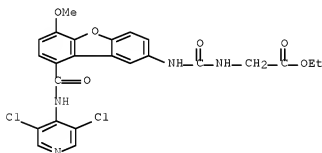
RN 778576-72-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]- (CA INDEX NAME)



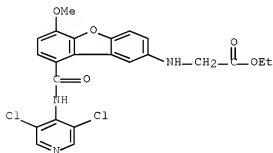
RN 778576-90-2 ZCAPLUS

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]-, ethyl ester (CA INDEX NAME)



RN 778576-92-4 ZCAPLUS

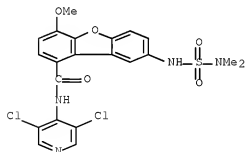
CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (CA INDEX NAME)



IT 778576-35-5P 778576-36-6P,

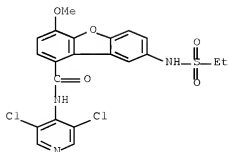
N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-38-8P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[{(3-chloropropyl)carbonyl}amino]dibenzo[b,d]furan-1-carboxamide
 778576-39-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-40-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[(tert-butylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide 778576-43-5P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778576-44-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-45-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-46-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [bis(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-47-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-48-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(isobutyl)oxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopropylmethoxycarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-51-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[[(trifluoromethyl)methoxy]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-52-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(diethylamino)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-53-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(cyclopentylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-55-9P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[N-methylpiperazin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 hydrochloride 778576-56-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[{(4-hydroxypiperidin-1-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-57-1P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[{(morpholin-4-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide 778576-58-2P
 , N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(isopropylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-59-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(hexylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-60-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(ethylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-61-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [(methylaminocarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-63-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778576-64-0P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(ethylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-65-1P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(dimethylamino)sulfonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-67-3P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[{(1-chloropropyl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-68-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(cyclopropylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide
 778576-71-9P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(hydroxycarbonylcarbonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt
 778576-73-1P, N-Phenyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-77-5P,
 N-(4-Methoxyphenyl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-80-0P, N-Benzyl-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide 778576-83-3P,

N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(ethylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-84-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 [[(butylamino)thiocarbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-85-5P, N-(Pyridin-3-yl)-4-methoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide 778576-87-7P
 778576-88-8P 778576-89-9P,
 N-(Pyridin-4-yl)-4-methoxy-8-acetamidodibenzo[b,d]furan-1-carboxamide
 778576-91-3P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-[[(2-
 hydroxy-2-oxoethyl)amino]carbonyl]amino]dibenzo[b,d]furan-1-carboxamide
 778576-93-5P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-(2-hydroxy-
 2-oxoethylamino)dibenzo[b,d]furan-1-carboxamide 778576-94-6P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-acetamido-9H-carbazole-4-
 carboxamide 778576-95-7P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(methylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-96-8P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-[(ethylsulfonyl)amino]-
 9H-carbazole-4-carboxamide 778576-97-9P,
 N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9-methyl-6-propionamido-9H-
 carbazole-4-carboxamide 778576-98-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [(methylsulfonyl)amino]dibenzo[b,d]furan-1-carboxamide disodium salt
 778576-99-1P 778577-06-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 acetamidodibenzo[b,d]furan-1-carboxamide sodium salt
 778577-07-4P, N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-
 [[(fur-2-yl)carbonyl]amino]dibenzo[b,d]furan-1-carboxamide sodium salt
 778581-69-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
 THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (PDE4 inhibitor; preparation of tricyclic heterocycles as PDE4
 inhibitors for treatment of immune and inflammatory disorders and
 insulin resistant diabetes)
 RN 778576-35-5 ZCAPLUS
 CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
 [[(dimethylamino)sulfonyl]amino]-4-methoxy- (CA INDEX NAME)



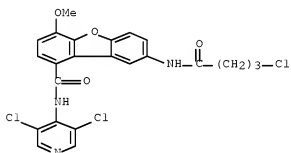
RN 778576-36-6 ZCAPLUS
 CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
 [(ethylsulfonyl)amino]-4-methoxy- (CA INDEX NAME)

10/524815



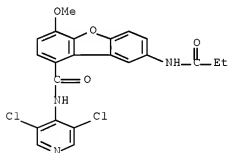
RN 778576-38-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(4-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-39-9 ZCAPLUS

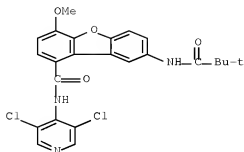
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(1-oxopropyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-40-2 ZCAPLUS

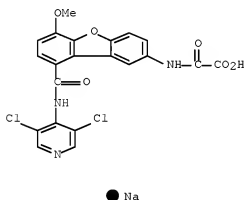
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2,2-dimethyl-1-oxopropyl)amino]-4-methoxy- (CA INDEX NAME)

10/524815



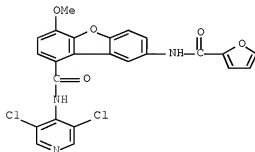
RN 778576-43-5 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:1) (CA INDEX NAME)



RN 778576-44-6 ZCAPLUS

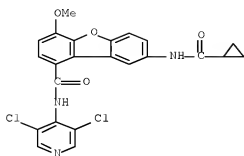
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[(2-furanylcarbonyl)amino]-4-methoxy- (CA INDEX NAME)



RN 778576-45-7 ZCAPLUS

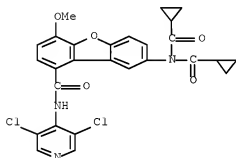
CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



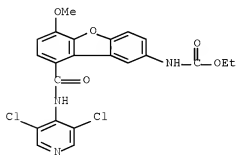
RN 778576-46-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[bis(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



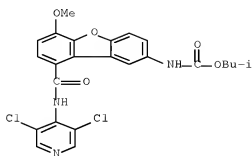
RN 778576-47-9 ZCAPLUS

CN Carbamic acid, [9-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, ethyl ester (9CI) (CA INDEX NAME)



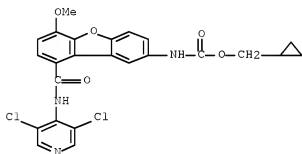
RN 778576-48-0 ZCAPLUS

CN Carbamic acid, [9-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2-methylpropyl ester (9CI) (CA INDEX NAME)



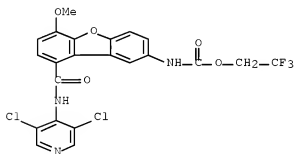
RN 778576-50-4 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, cyclopropylmethyl ester (9CI) (CA INDEX NAME)



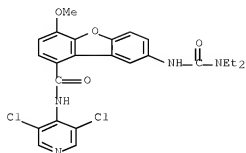
RN 778576-51-5 ZCAPLUS

CN Carbamic acid, [9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-, 2,2,2-trifluoroethyl ester (9CI) (CA INDEX NAME)



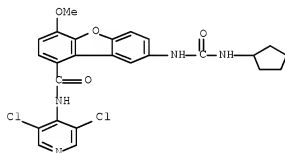
RN 778576-52-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[[(diethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



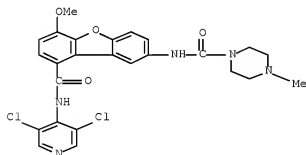
RN 778576-53-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[[(cyclopentylamino)carbonyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-55-9 ZCAPLUS

CN 1-Piperazinecarboxamide, N-[9-[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-methyl-, hydrochloride (1:1) (CA INDEX NAME)

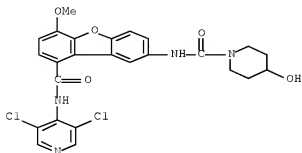


● HCl

RN 778576-56-0 ZCAPLUS

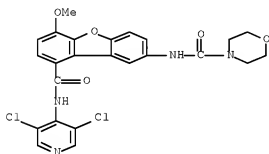
10/524815

CN 1-Piperidinecarboxamide, N-[9-[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]-4-hydroxy- (CA INDEX NAME)



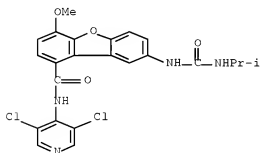
RN 778576-57-1 ZCAPLUS

CN 4-Morpholinecarboxamide, N-[9-[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)



RN 778576-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[[(1-methylethyl)amino]carbonyl]amino]- (CA INDEX NAME)

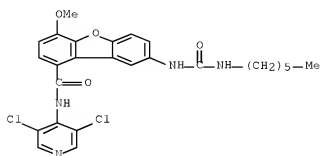


RN 778576-59-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-

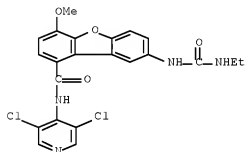
10/524815

[[(hexylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



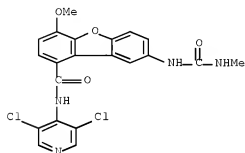
RN 778576-60-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-
[[(ethylamino)carbonyl]amino]-4-methoxy- (CA INDEX NAME)



RN 778576-61-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-
[[(methylamino)carbonyl]amino]- (CA INDEX NAME)

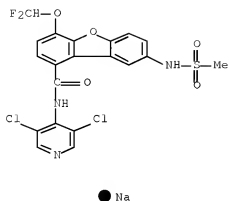


RN 778576-63-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-
(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:1) (CA INDEX

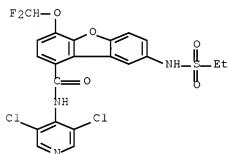
10/524815

NAME)



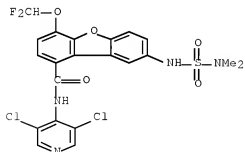
RN 778576-64-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(ethylsulfonyl)amino]- (CA INDEX NAME)



RN 778576-65-1 ZCAPLUS

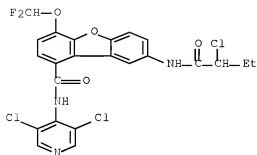
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[[dimethylamino)sulfonyl]amino]- (CA INDEX NAME)



10/524815

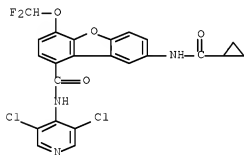
RN 778576-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(2-chloro-1-oxobutyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



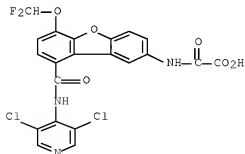
RN 778576-68-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[(cyclopropylcarbonyl)amino]-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



RN 778576-71-9 ZCAPLUS

CN Acetic acid, 2-[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-(difluoromethoxy)-2-dibenzofuranyl]amino]-2-oxo-, sodium salt (1:2) (CA INDEX NAME)

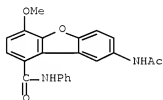


● 2 Na

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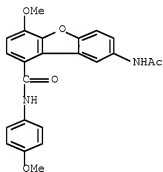
RN 778576-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-phenyl- (CA INDEX NAME)



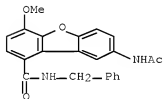
RN 778576-77-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



RN 778576-80-0 ZCAPLUS

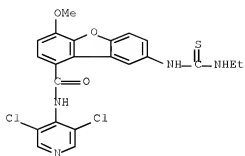
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-(phenylmethyl)- (CA INDEX NAME)



RN 778576-83-3 ZCAPLUS

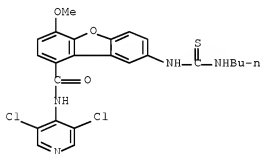
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-[[(ethylamino)thioxomethyl]amino]-4-methoxy- (CA INDEX NAME)

10/524815



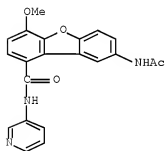
RN 778576-84-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-[[[(butylamino)thioxomethyl]amino]-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 778576-85-5 ZCAPLUS

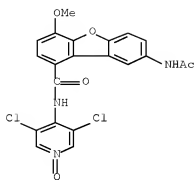
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 778576-87-7 ZCAPLUS

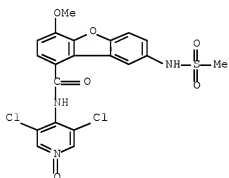
CN 1-Dibenzofurancarboxamide, 8-(acetylamino)-N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



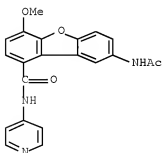
RN 778576-88-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-[(methylsulfonyl)amino]- (CA INDEX NAME)



RN 778576-89-9 ZCAPLUS

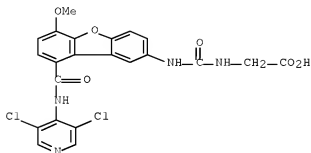
CN 1-Dibenzofurancarboxamide, 8-(acetyl amino)-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 778576-91-3 ZCAPLUS

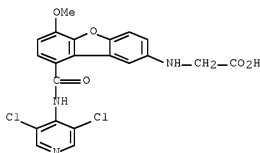
10/524815

CN Glycine, N-[[[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]amino]carbonyl]- (CA INDEX NAME)



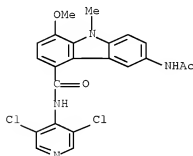
RN 778576-93-5 ZCAPLUS

CN Glycine, N-[9-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-6-methoxy-2-dibenzofuranyl]- (CA INDEX NAME)



RN 778576-94-6 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-(acetylamino)-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl- (CA INDEX NAME)

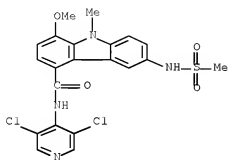


RN 778576-95-7 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-

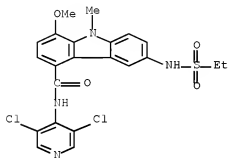
10/524815

methyl-6-[(methylsulfonyl)amino]- (CA INDEX NAME)



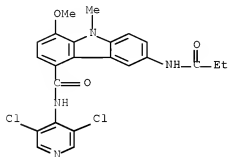
RN 778576-96-8 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-6-[(ethylsulfonyl)amino]-1-methoxy-9-methyl- (CA INDEX NAME)



RN 778576-97-9 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-methyl-6-[(1-oxopropyl)amino]- (CA INDEX NAME)

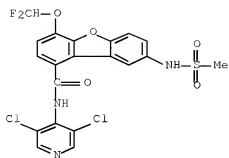


RN 778576-98-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(methylsulfonyl)amino]-, sodium salt (1:2) (CA INDEX NAME)

10/524815

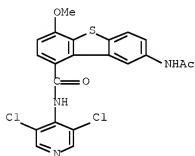
NAME)



●2 Na

RN 778576-99-1 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 8-(acetamino)-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-, sodium salt (1:2) (CA INDEX NAME)

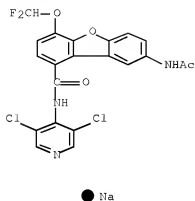


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RN 778577-06-3 ZCAPLUS

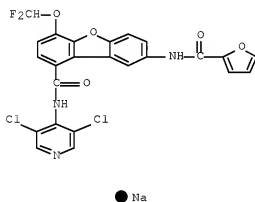
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10/524815



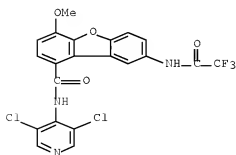
RN 778577-07-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-[(2-furanylcarbonyl)amino]-, sodium salt (1:1) (CA INDEX NAME)



RN 778581-69-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-[(2,2,2-trifluoroacetyl)amino]- (CA INDEX NAME)



OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD
(7 CITINGS)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

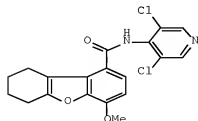
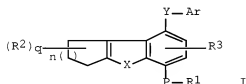
L74 ANSWER 4 OF 7 ZCAPLUS COPYRIGHT 2009 ACS ON STN
ACCESSION NUMBER: 2004:675744 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:207059

TITLE: Tricyclic compounds (dibenzofurans, dibenzothiophenes, carbazoles, and analogs) with PDE4 inhibitory activity, useful for the treatment of inflammatory and allergic disorders, process for their preparation, and methods of use

INVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram; Lakdawala, Aftab Dawoodbhai; Bedekar, Sarika Suhas
PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069831	A1	20040819	WO 2004-IB330	20040210 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, RW, BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00177	A	20050204	IN 2003-MU177	20030210 <--
PRIORITY APPLN. INFO.:			IN 2003-MU177	A 20030210 <--
OTHER SOURCE(S):		MARPAT 141:207059		
GI				



- AB The invention relates to novel heterocyclic compds. and their analogs, tautomers, regioisomers, stereoisomers, enantiomers, diastereomers, polymorphs, pharmaceutically acceptable salts, appropriate oxides, and pharmaceutically acceptable solvates, as well as pharmaceutical compns. containing them. The invention more particularly relates to novel phosphodiesterase type 4 (PDE4) inhibitors. In particular, compds. I and their aforementioned related compds. are claimed [wherein: R1, R2, R3 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, protecting groups, or two ortho R2 may form 3- to 7-membered ring with 0-2 optional NR1/O/S heteroatoms; X = O, S(O)m, NH, or NR5; Y = CONR4, NR4SO2, SO2NR4, and NR4CO; P = O or S; q = 0-5; n = 1-3; m = 0-2; Ar = (un)substituted aryl, arylalkyl, heterocyclic, or heteroaryl; R4 = H, (un)substituted alkyl, OH, OR1, aryl, or heterocyclic; R5 = (un)substituted alk(en/yn)yl, cycloalk(en)yl, cycloalkylalkyl, (hetero)aryl, (hetero)arylalkyl, heterocyclyl(alkyl), COR1, COOR1, CONR1R1, S(O)mR1, S(O)mNR1R1, NO2, OH, cyano, amino, formyl, acetyl, halo, OR1, SR1, and protecting groups]. The compds. (33 examples) were prepared and tested for PDE4 inhibitory activity. For instance, 6-methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-carboxylic acid chloride [prepared in 5 steps from 2-methoxyphenol (guaiacol) and 2-bromocyclohexanone] was amidated with 4-amino-3,5-dichloropyridine in DMF/THF to give invention compound II. This compound had an IC50 value of 0.4468 nM against PDE4 in vitro.
- IC ICM C07D405-12
ICS C07D409-12; C07D401-12; C07D307-92; A61K031-343; A61K031-381; A61K031-403
- CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
- ST tricyclic prepn phosphodiesterase 4 inhibitor antiinflammatory
antiallergic; pyridyl dibenzofuran dibenzothiophene carbazole PDE4
inhibitor inflammation allergy treatment
- IT Alzheimer's disease
Amnesia
Asthma
Central nervous system, disease
Cystic fibrosis
Eczema
Gout
Immune disease
Inflammation
Multiple sclerosis
Osteoarthritis
Psoriasis
Respiratory distress syndrome
Rheumatoid arthritis
Shock (circulatory collapse)
Urticaria
(treatment of; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)
- IT 740872-01-9P, 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-ylcarboxamido)pyridine
740872-02-0P, 4-(6-Methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-03-1P,
3-(6-Methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-ylcarboxamido)pyridine
740872-04-2P, 4-(6-Methoxy-1,2,3,4-tetrahydrobenzo[b,d]furan-9-

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 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine N-oxide 740872-06-4P,
 (±)-3,5-Dichloro-4-(6-methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-07-5P, (±)-4-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-08-6P, (±)-3-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-09-7P, 3,5-Dichloro-4-(6-difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-10-0P, 4-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-11-1P, 3-(6-Difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-12-2P, 3,5-Dichloro-4-(6-cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-13-3P, 4-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-14-4P, 3-(6-Cyclopropylmethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-15-5P, 3,5-Dichloro-4-(6-ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-16-6P, 3-(6-Ethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-17-7P, 3,5-Dichloro-4-(6-isopropoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-18-8P, 3,5-Dichloro-4-(6-cyclopentylloxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-19-9P, 3,5-Dichloro-4-[4-methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-20-2P, 4-[4-Methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-21-3P, 3-[4-Methoxy-7,8,9,10-tetrahydro-6H-benzo[b]cyclohepta[d]furan-9-carboxamido]pyridine 740872-22-4P, 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-23-5P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-24-6P, N5-(4-Pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-25-7P, N5-(3,5-Dichloro-4-pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-26-8P, N5-(4-Pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-27-9P, N5-(3,5-Dichloro-4-pyridyl)-9-cyclohexylmethyl-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-28-0P, N5-(4-Pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-29-1P, N5-(4-Methoxyphenyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-30-4P, N5-(3,5-Dichloro-4-pyridyl)-9-(4-fluorobenzyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide 740872-31-5P, N1-(4-Pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-32-6P, N1-(3,5-Dichloro-4-pyridyl)-4-methoxy-5,6,7,8,9,10-hexahydrocyclohepta[b]indole-1-carboxamide 740872-33-7P, N8-(3,5-Dichloro-4-pyridyl)-5-methoxy-1,2,3,4-tetrahydrocyclopenta[b]indole-8-carboxamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(drug candidate; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

IT 740872-01-9P, 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine
 740872-02-0P, 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine 740872-03-1P,
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 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine N-oxide 740872-06-4P,
 (±)-3,5-Dichloro-4-(6-methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine
 740872-07-5P, (±)-4-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine
 740872-08-6P, (±)-3-(6-Methoxy-3-methyl-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine
 740872-09-7P, 3,5-Dichloro-4-(6-difluoromethoxy-1,2,3,4-tetrahydrodibenzo[b,d]furan-9-ylcarboxamido)pyridine
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 3,5-Dichloro-4-(6-methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-23-5P,
 4-(6-Methoxy-1,2,3,4-tetrahydrodibenzo[b,d]thiophen-9-ylcarboxamido)pyridine 740872-24-6P,
 N5-(4-Pyridyl)-8-methoxy-2,3,4,9-tetrahydro-1H-5-carbazolecarboxamide
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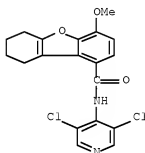
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 N8-(3,5-Dichloro-4-pyridyl)-5-methoxy-1,2,3,4-tetrahydrocyclopenta[b]indole-8-carboxamide
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of dibenzofurans, dibenzothiophenes, carbazoles, and analogs with PDE4 inhibitory activity, for treatment of inflammatory and allergic disorders)

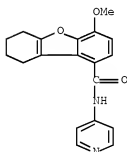
RN 740872-01-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-methoxy- (CA INDEX NAME)



RN 740872-02-0 ZCAPLUS

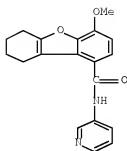
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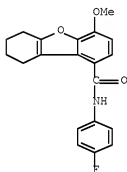
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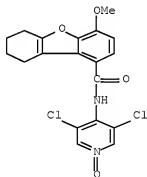
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(CA INDEX NAME)



RN 740872-05-3 ZCAPLUS

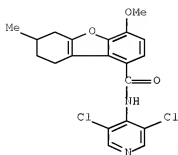
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RN 740872-06-4 ZCAPLUS

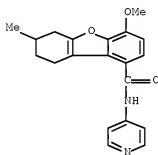
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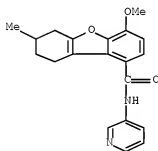
RN 740872-07-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 6,7,8,9-tetrahydro-4-methoxy-7-methyl-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-08-6 ZCAPLUS

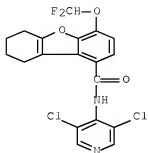
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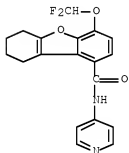
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10/524815



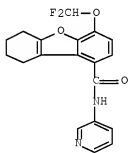
RN 740872-10-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-6,7,8,9-tetrahydro-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-11-1 ZCAPLUS

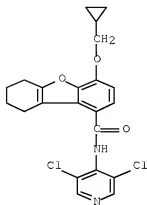
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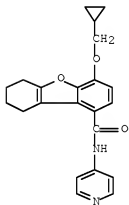
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10/524815



RN 740872-13-3 ZCAPLUS

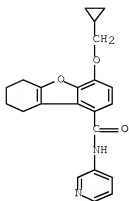
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RN 740872-14-4 ZCAPLUS

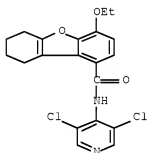
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10/524815



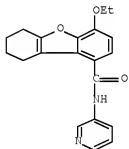
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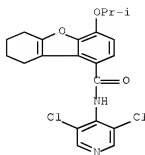
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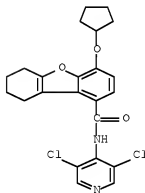
RN 740872-17-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-(1-methylethoxy)- (CA INDEX NAME)



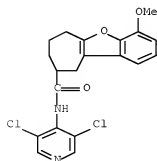
RN 740872-18-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro- (CA INDEX NAME)



RN 740872-19-9 ZCAPLUS

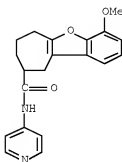
CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide, N-(3,5-dichloro-4-pyridinyl)-7,8,9,10-tetrahydro-4-methoxy- (CA INDEX NAME)



10/524815

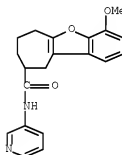
RN 740872-20-2 ZCAPLUS

CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide,
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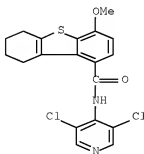
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CN 6H-Benzo[b]cyclohepta[d]furan-9-carboxamide,
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RN 740872-22-4 ZCAPLUS

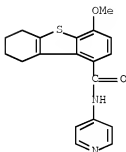
CN 1-Dibenzothiophenecarboxamide, N-(3,5-dichloro-4-pyridinyl)-6,7,8,9-tetrahydro-4-methoxy- (CA INDEX NAME)



10/524815

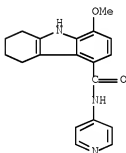
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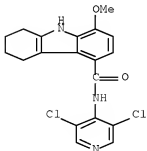
RN 740872-24-6 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl-
(CA INDEX NAME)



RN 740872-25-7 ZCAPLUS

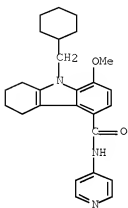
CN 1H-Carbazole-5-carboxamide, N-(3,5-dichloro-4-pyridinyl)-2,3,4,9-
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10/524815

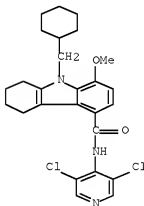
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CN 1H-Carbazole-5-carboxamide, 9-(cyclohexylmethyl)-2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl- (CA INDEX NAME)



RN 740872-27-9 ZCAPLUS

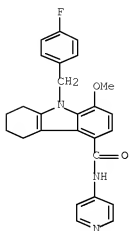
CN 1H-Carbazole-5-carboxamide, 9-(cyclohexylmethyl)-N-(3,5-dichloro-4-pyridinyl)-2,3,4,9-tetrahydro-8-methoxy- (CA INDEX NAME)



RN 740872-28-0 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy-N-4-pyridinyl- (CA INDEX NAME)

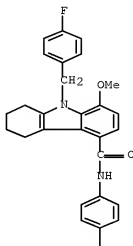
10/524815



RN 740872-29-1 ZCAPLUS

CN 1H-Carbazole-5-carboxamide, 9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)

PAGE 1-A

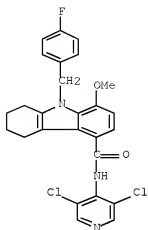


PAGE 2-A



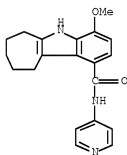
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CN 1H-Carbazole-5-carboxamide, N-(3,5-dichloro-4-pyridinyl)-9-[(4-fluorophenyl)methyl]-2,3,4,9-tetrahydro-8-methoxy- (CA INDEX NAME)



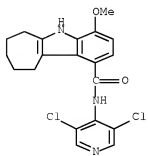
RN 740872-31-5 ZCAPLUS

CN Cyclohept[b]indole-1-carboxamide, 5,6,7,8,9,10-hexahydro-4-methoxy-N-(4-pyridinyl)- (CA INDEX NAME)



RN 740872-32-6 ZCAPLUS

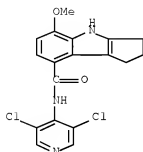
CN Cyclohept[b]indole-1-carboxamide, N-(3,5-dichloro-4-pyridinyl)-5,6,7,8,9,10-hexahydro-4-methoxy- (CA INDEX NAME)



10/524815

RN 740872-33-7 ZCAPLUS

CN Cyclopent[b]indole-8-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,2,3,4-tetrahydro-5-methoxy- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 5 OF 7 ZCAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2004:370918 ZCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:391192

TITLE: Preparation of dibenzofuran/dibenzothiophene
derivatives useful for the treatment of inflammatory
and allergic disordersINVENTOR(S): Balasubramanian, Gopalan; Gharat, Laxmikant Atmaram;
Lakdawala, Aftab Dawoodbhai; Anupindi, Raghu Ram

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Ltd., India

SOURCE: PCT Int. Appl., 254 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

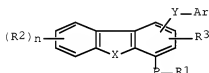
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037805	A1	20040506	WO 2003-IB4442	20031008 <--
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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IN 2002MU00922	A	20050304	IN 2002-MU922	20021023 <--
CA 2503015	A1	20040506	CA 2003-2503015	20031008 <--
AU 2003269317	A1	20040513	AU 2003-269317	20031008 <--
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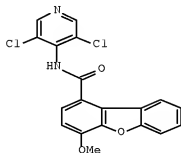
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BR 2003014721	A	20050802 BR 2003-14721 20031008 <--
CN 1729181	A	20060201 CN 2003-80107246 20031008 <--
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ES 2298552	T3	20080516 ES 2003-751096 20031008 <--
ZA 2005002969	A	20060222 ZA 2005-2969 20050413 <--
US 20060178418	A1	20060810 US 2005-532273 20050926 <--
US 7238725	B2	20070703
US 20080146810	A1	20080619 US 2007-769074 20070627 <--
PRIORITY APPLN. INFO.:		IN 2002-MU922 A 20021023 <--
		WO 2003-IB4442 W 20031008 <--
		US 2005-532273 A1 20050926

OTHER SOURCE(S): MARPAT 140:391192

GI



I



II

AB Title compds. I [R1-3 = H, alk(en/yn)yl, cycloalkyl, etc.; P = O, S; n = 0-4; Ar = (un)substituted aryl, etc.; Y = carboxamido, aminosulfonyl, etc.] are prepared For instance, 4-methoxydibenzofuran-1-carboxylic acid (preparation given) is converted to the corresponding acid chloride (PhH, SOCl₂, reflux, 4 h) and treated with 4-amino-3,5-dichloropyridine (DMF/THF, NaH, -10°) to give II. II has IC₅₀ = 0.8 nM for PDE4. I are useful for the treatment of inflammatory conditions, diseases of the central nervous and insulin resistant diabetes.

IC ICM C07D307-91
ICS C07D333-76; C07D209-88; C07D405-12; C07D401-12; C07D409-12;
C07D405-14; A61K031-403; A61K031-34; A61K031-381; A61P037-00;
A61P025-00; A61P003-10

CC 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

ST tricyclic dibenzofuran dibenzothiophene inflammatory allergic process
prepn

IT Alzheimer's disease
Amnesia
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidepressants
Antidiabetic agents
Antirheumatic agents
Asthma
Cystic fibrosis
Diabetes insipidus

Diabetes mellitus
 Gout
 Human
 Immune disease
 Inflammation
 Multiple sclerosis
 Nervous system agents
 Osteoarthritis
 Psoriasis
 Respiratory distress syndrome
 Rheumatoid arthritis

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

- II 685874-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-44-6P,
 N-(Pyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-48-0P, N-(Pyridin-3-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 trifluoromethylidibenzofuran-1-carboxamide 685874-53-7P,
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 carboxamide 685875-04-1P,
 3,5-Dichloro-4-(4-ethoxydibenzofuran-1-ylcarboxamido)pyridine
 685875-07-4P, 3,5-Dichloro-4-(4-cyclopentylmethoxydibenzofuran-1-
 ylcarboxamido)pyridine 685875-14-3P,
 N-Formyl-1-methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole
 685875-16-5P, N-Formyl-1-methoxy-4-(((4-
 methylphenyl)amino)sulfonyl)-9H-carbazole 685875-17-6P,
 1-Methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole
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 685875-80-3P, N-(4-Methoxyphenyl)-4-methoxydibenzothiophene-1-
 carboxamide 685875-97-2P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment
 of inflammatory and allergic disorders)
- II 685874-43-5P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-

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 685874-46-8P, N-(2-Chloropyridin-3-yl)-4-methoxydibenzofuran-1-
 carboxamide 685874-47-9P,
 N-(4-Fluorophenyl)-4-methoxydibenzofuran-1-carboxamide
 685874-49-1P, N-(1-Oxopyridin-3-yl)-4-methoxydibenzofuran-1-
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 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-
 1-carboxamide 685874-52-6P,
 N-(Pyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-1-carboxamide
 685874-54-8P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxy-
 8-trifluoromethylidibenzofuran-1-carboxamide 685874-56-0P,
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
 carboxamide 685874-58-2P,
 N-(1-Oxopyridin-3-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
 carboxamide 685874-59-3P,
 N-(Pyridin-2-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
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 carboxamide 685874-91-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-ethoxycarbomethoxydibenzofuran-1-
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 aminodibenzofuran-1-carboxamide 685874-99-1P,

N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685875-00-7P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-cyanodibenzofuran-1-carboxamide 685875-05-2P, N-Benzyl-4-cyclopentylloxidibenzofuran-1-carboxamide 685875-06-3P, 4-[4-((Cyclopentyl)oxy)dibenzofuran-1-ylcarboxamido]pyridine 685875-08-5P,
 4-(4-Methylsulfanyldibenzofuran-1-ylcarboxamido)pyridine 685875-09-6P, N-(4-Methoxydibenzofuran-1-yl)nicotinamide 685875-10-9P, N-Benzyl-4-methoxydibenzofuran-1-sulfonamide 685875-11-0P, 4-(((4-Methoxydibenzofuran-1-yl)sulfonyl)amino)pyridine 685875-12-1P 685875-13-2P 685875-15-4P, 1-Methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole 685875-20-1P 685875-21-2P,
 1-Methoxy-4-(((pyridin-4-yl)amino)sulfonyl)-9H-carbazole 685875-22-3P, N-(2,6-Dichlorophenyl)-1-methoxy-9H-4-carbazolsulfonamide 685875-23-4P,
 N-(2,6-Dichlorophenyl)-9-formyl-1-methoxy-9H-4-carbazolsulfonamide 685875-24-5P, N-(Pyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide 685875-25-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide 685875-26-7P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9H-4-carbazolecarboxamide 685875-30-3P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-methoxy-9H-4-carbazolecarboxamide 685875-32-5P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-carbazolecarboxamide 685875-34-7P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-36-9P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-38-1P,
 N-(3,5-Dichloropyridin-4-yl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-41-6P,
 N-(4-Pyridyl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-44-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-methoxy-9H-4-carbazolecarboxamide 685875-48-3P,
 N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide 685875-52-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-ethoxy-9H-4-carbazolecarboxamide 685875-56-3P,
 N-(4-Pyridyl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide 685875-57-4P, N-(3-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-58-5P,
 N-(4-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-59-6P,
 N-(3,5-Dichloropyridin-4-yl)-8-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-carbazolecarboxamide 685875-63-2P,
 N-(3,5-Dichloropyridin-4-yl)-8-chloro-9-(4-Fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-67-6P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9-methyl-9H-4-carbazolecarboxamide 685875-71-2P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-72-3P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-carbazolecarboxamide 685875-73-4P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-carbazolecarboxamide 685875-74-5P,
 N-(3,5-Dichloropyridin-4-yl)-9-methyl-1-methoxy-9H-4-carbazolecarboxamide 685875-81-4P 685875-82-5P,
 N-(4-Chlorophenyl)-4-methoxydibenzothiophene-1-carboxamide 685875-83-6P 685875-84-7P 685875-85-8P
 685875-86-9P 685875-87-0P 685875-89-2P
 685875-90-5P 685875-92-7P 685875-93-8P

685875-94-9P 685875-98-3P 685875-99-4P
 685876-00-0P 685876-01-1P 685876-02-2P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-(2-oxopyrrolidin-1-yl)dibenzofuran-1-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

IT 685874-42-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-44-6P,
 N-(Pyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-48-0P, N-(Pyridin-3-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-50-4P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-1-carboxamide 685874-53-7P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-carboxamide 685874-55-9P,
 N-(Pyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-carboxamide 685874-57-1P,
 N-(Pyridin-3-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-carboxamide 685874-60-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-61-7P, N-(Pyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-63-9P,
 N-(Pyridin-3-yl)-4-difluoromethoxydibenzofuran-1-carboxamide 685874-66-2P, N-(3,5-Dichloropyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-68-4P,
 N-(Pyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-70-8P, N-(Pyridin-3-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide 685874-72-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-74-2P, N-(Pyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-76-4P,
 N-(Pyridin-3-yl)-4-isopropoxydibenzofuran-1-carboxamide 685874-79-7P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-nitrodibenzofuran-1-carboxamide 685875-02-9P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-nitrodibenzofuran-1-carboxamide 685875-03-0P,
 N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-aminodibenzofuran-1-carboxamide 685875-04-1P,
 3,5-Dichloro-4-(4-ethoxydibenzofuran-1-ylcarboxamido)pyridine 685875-07-4P, 3,5-Dichloro-4-(4-cyclopentylmethoxydibenzofuran-1-ylcarboxamido)pyridine 685875-14-3P,
 N-Formyl-1-methoxy-4-(((4-methoxyphenyl)amino)sulfonyl)-9H-carbazole 685875-16-5P, N-Formyl-1-methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole 685875-17-6P,
 1-Methoxy-4-(((4-methylphenyl)amino)sulfonyl)-9H-carbazole 685875-18-7P 685875-78-9P 685875-79-0P
 685875-80-3P, N-(4-Methoxyphenyl)-4-methoxydibenzothiophene-1-carboxamide 685875-97-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN

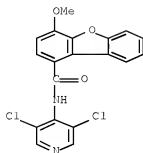
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

RN 685874-42-4 ZCAPLUS

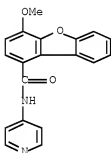
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)

10/524815



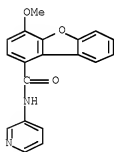
RN 685874-44-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



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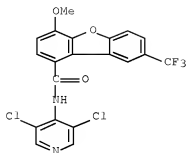
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RN 685874-50-4 ZCAPLUS

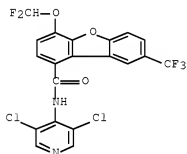
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



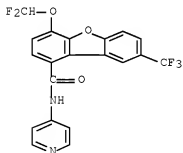
RN 685874-53-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-(trifluoromethyl)- (CA INDEX NAME)



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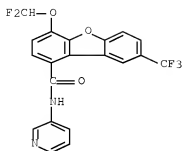
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-4-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-57-1 ZCAPLUS

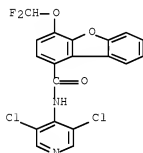
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-3-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



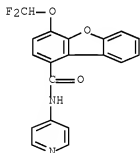
RN 685874-60-6 ZCAPLUS

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RN 685874-61-7 ZCAPLUS

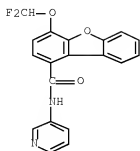
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-4-pyridinyl- (CA INDEX NAME)



RN 685874-63-9 ZCAPLUS

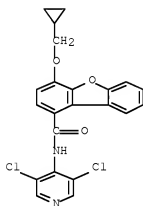
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-3-pyridinyl- (CA INDEX NAME)

10/524815



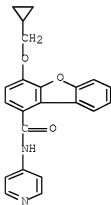
RN 685874-66-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(3,5-dichloro-4-pyridinyl)- (CA INDEX NAME)



RN 685874-68-4 ZCAPLUS

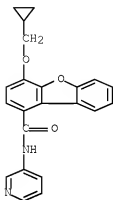
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-4-pyridinyl- (CA INDEX NAME)



10/524815

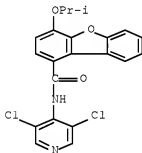
RN 685874-70-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-3-pyridinyl- (CA INDEX NAME)



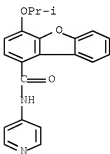
RN 685874-72-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(1-methylethoxy)- (CA INDEX NAME)



RN 685874-74-2 ZCAPLUS

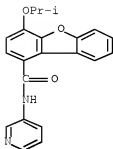
CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-4-pyridinyl- (CA INDEX NAME)



10/524815

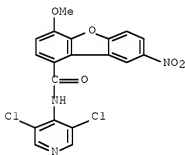
RN 685874-76-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-3-pyridinyl- (CA INDEX NAME)



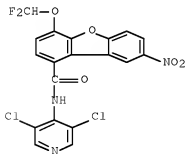
RN 685874-79-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy-8-nitro- (CA INDEX NAME)



RN 685875-02-9 ZCAPLUS

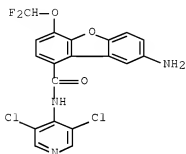
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)-8-nitro- (CA INDEX NAME)



10/524815

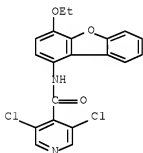
RN 685875-03-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-amino-N-(3,5-dichloro-4-pyridinyl)-4-(difluoromethoxy)- (CA INDEX NAME)



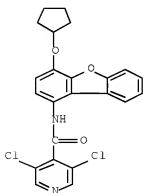
RN 685875-04-1 ZCAPLUS

CN 4-Pyridinecarboxamide, 3,5-dichloro-N-(4-ethoxy-1-dibenzofuranyl)- (CA INDEX NAME)



RN 685875-07-4 ZCAPLUS

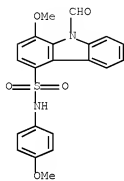
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(cyclopentyloxy)-1-dibenzofuranyl]- (CA INDEX NAME)



10/524815

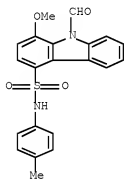
RN 685875-14-3 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 9-formyl-1-methoxy-N-(4-methoxyphenyl)- (CA
INDEX NAME)



RN 685875-16-5 ZCAPLUS

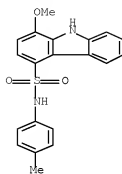
CN 9H-Carbazole-4-sulfonamide, 9-formyl-1-methoxy-N-(4-methylphenyl)- (CA
INDEX NAME)



RN 685875-17-6 ZCAPLUS

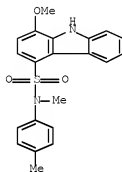
CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N-(4-methylphenyl)- (CA INDEX NAME)

10/524815



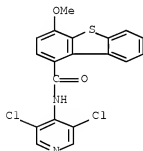
RN 685875-18-7 ZCAPLUS

CN 9H-Carbazole-4-sulfonamide, 1-methoxy-N-methyl-N-(4-methylphenyl)- (CA INDEX NAME)



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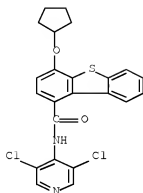
CN 1-Dibenzothiophenecarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 685875-79-0 ZCAPLUS

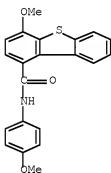
CN 1-Dibenzothiophenecarboxamide, 4-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridinyl)- (CA INDEX NAME)

10/524815



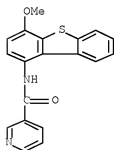
RN 685875-80-3 ZCAPLUS

CN 1-Dibenzothiophenecarboxamide, 4-methoxy-N-(4-methoxyphenyl)- (CA INDEX NAME)



RN 685875-97-2 ZCAPLUS

CN 3-Pyridinecarboxamide, N-(4-methoxy-1-dibenzothienyl)- (CA INDEX NAME)



IT 685874-43-5P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide 685874-45-7P,

N-(1-Oxopyridin-4-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-46-8P, N-(2-Chloropyridin-3-yl)-4-methoxydibenzofuran-1-
 carboxamide 685874-47-9P,
 N-(4-Fluorophenyl)-4-methoxydibenzofuran-1-carboxamide
 685874-49-1P, N-(1-Oxopyridin-3-yl)-4-methoxydibenzofuran-1-
 carboxamide 685874-51-5P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-
 1-carboxamide 685874-52-6P,
 N-(Pyridin-4-yl)-4-methoxy-8-trifluoromethylidibenzofuran-1-carboxamide
 685874-54-8P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxy-
 8-trifluoromethylidibenzofuran-1-carboxamide 685874-56-0P,
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
 carboxamide 685874-58-2P,
 N-(1-Oxopyridin-3-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
 carboxamide 685874-59-3P,
 N-(Pyridin-2-yl)-4-difluoromethoxy-8-trifluoromethylidibenzofuran-1-
 carboxamide 685874-62-8P,
 N-(1-Oxopyridin-4-yl)-4-difluoromethoxydibenzofuran-1-carboxamide
 685874-64-0P, N-(1-Oxopyridin-3-yl)-4-difluoromethoxydibenzofuran-
 1-carboxamide 685874-65-1P,
 N-(5-Chloropyridin-2-yl)-4-difluoromethoxydibenzofuran-1-carboxamide
 685874-67-3P, N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-
 cyclopropylmethoxydibenzofuran-1-carboxamide 685874-69-5P,
 N-(1-Oxopyridin-4-yl)-4-cyclopropylmethoxydibenzofuran-1-carboxamide
 685874-71-9P, N-(1-Oxopyridin-3-yl)-4-
 cyclopropylmethoxydibenzofuran-1-carboxamide 685874-73-1P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-isopropoxydibenzofuran-1-
 carboxamide 685874-75-3P,
 N-(1-Oxopyridin-4-yl)-4-isopropoxydibenzofuran-1-carboxamide
 685874-77-5P, N-(1-Oxopyridin-3-yl)-4-isopropoxydibenzofuran-1-
 carboxamide 685874-78-6P,
 N-(3,5-Dichloropyridin-4-yl)-4-benzyloxydibenzofuran-1-carboxamide
 685874-80-0P, N-(Pyridin-4-yl)-4-methoxy-8-nitrodibenzofuran-1-
 carboxamide 685874-81-1P,
 N-(Pyridin-3-yl)-4-methoxy-8-nitrodibenzofuran-1-carboxamide
 685874-82-2P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 chlorodibenzofuran-1-carboxamide 685874-83-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide
 685874-84-4P, N-(Pyridin-4-yl)-4-methoxy-8-bromodibenzofuran-1-
 carboxamide 685874-85-5P,
 N-(Pyridin-3-yl)-4-methoxy-8-bromodibenzofuran-1-carboxamide
 685874-86-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 iododibenzofuran-1-carboxamide 685874-87-7P,
 N-(Pyridin-4-yl)-4-methoxy-8-iododibenzofuran-1-carboxamide
 685874-88-8P, N-(Pyridin-3-yl)-4-methoxy-8-iododibenzofuran-1-
 carboxamide 685874-89-9P,
 N-(4-Methylpyrimidin-2-yl)-4-methoxydibenzofuran-1-carboxamide
 685874-90-2P, N-(2,5-Dichlorophenyl)-4-methoxydibenzofuran-1-
 carboxamide 685874-91-3P,
 N-(3,5-Dichloropyridin-4-yl)-4-ethoxycarbomethoxydibenzofuran-1-
 carboxamide 685874-92-4P,
 N-(3,5-Dichloropyridin-4-yl)-4-[(carboxy)methoxy]dibenzofuran-1-
 carboxamide 685874-93-5P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-2-carboxamide
 685874-94-6P, N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-3-
 carboxamide 685874-95-7P 685874-96-8P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxydibenzofuran-1-sulfonamide
 685874-98-0P, N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-
 aminodibenzofuran-1-carboxamide 685874-99-1P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-4-difluoromethoxydibenzofuran-1-

carboxamide 685875-00-7P,
 N-(3,5-Dichloropyridin-4-yl)-4-methoxy-8-cyanodibenzofuran-1-carboxamide
 685875-05-2P, N-Benzyl-4-cyclopentyl oxydibenzofuran-1-carboxamide
 685875-06-3P, 4-[4-((Cyclopentyl)oxy)dibenzofuran-1-
 ylcarboxamido]pyridine 685875-08-5P,
 4-(4-Methylsulfonyldibenzofuran-1-ylcarboxamido)pyridine
 685875-09-6P, N-(4-Methoxydibenzofuran-1-yl)nicotinamide
 685875-10-9P, N-Benzyl-4-methoxydibenzofuran-1-sulfonamide
 685875-11-0P, 4-(((4-Methoxydibenzofuran-1-
 yl)sulfonyl)amino)pyridine 685875-12-1P 685875-13-2P
 685875-15-4P, 1-Methoxy-4-(((4-Methoxyphenyl)amino)sulfonyl)-9H-
 carbazole 685875-20-1P 685875-21-2P,
 1-Methoxy-4-(((pyridin-4-yl)amino)sulfonyl)-9H-carbazole
 685875-22-3P, N-(2,6-Dichlorophenyl)-1-methoxy-9H-4-
 carbazolsulfonamide 685875-23-4P,
 N-(2,6-Dichlorophenyl)-9-formyl-1-methoxy-9H-4-carbazolsulfonamide
 685875-24-5P, N-(Pyridin-4-yl)-1-methoxy-9H-4-carbazolecarboxamide
 685875-25-6P, N-(3,5-Dichloropyridin-4-yl)-1-methoxy-9H-4-
 carbazolecarboxamide 685875-26-7P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9H-4-carbazolecarboxamide
 685875-30-3P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-
 methoxy-9H-4-carbazolecarboxamide 685875-32-5P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-
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 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-
 carbazolecarboxamide 685875-36-9P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-9H-4-
 carbazolecarboxamide 685875-38-1P,
 N-(3,5-Dichloropyridin-4-yl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-
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 N-(4-Pyridyl)-9-(4-fluorobenzyl)-1-methoxy-9H-4-carbazolecarboxamide
 685875-44-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-methoxy-9H-4-
 carbazolecarboxamide 685875-48-3P,
 N-(3,5-Dichloropyridin-4-yl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide
 685875-52-9P, N-(3,5-Dichloropyridin-4-yl)-9-benzyl-6-chloro-1-
 ethoxy-9H-4-carbazolecarboxamide 685875-56-3P,
 N-(4-Pyridyl)-9-benzyl-1-ethoxy-9H-4-carbazolecarboxamide
 685875-57-4P, N-(3-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-
 9H-4-carbazolecarboxamide 685875-58-5P,
 N-(4-Pyridyl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-9H-4-
 carbazolecarboxamide 685875-59-6P,
 N-(3,5-Dichloropyridin-4-yl)-8-chloro-9-cyclohexylmethyl-1-methoxy-9H-4-
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 carbazolecarboxamide 685875-67-6P,
 N-(3,5-Dichloropyridin-4-yl)-6-chloro-1-methoxy-9-methyl-9H-4-
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 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-fluorobenzyl)-1-methoxy-
 9H-4-carbazolecarboxamide 685875-72-3P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-(4-methoxybenzyl)-1-methoxy-
 9H-4-carbazolecarboxamide 685875-73-4P,
 N-(1-Oxo-3,5-dichloropyridin-4-yl)-6-chloro-9-cyclohexylmethyl-1-methoxy-
 9H-4-carbazolecarboxamide 685875-74-5P,
 N-(3,5-Dichloropyridin-4-yl)-9-methyl-1-methoxy-9H-4-carbazolecarboxamide
 685875-81-4P 685875-82-5P,
 N-(4-Chlorophenyl)-4-methoxydibenzothiophene-1-carboxamide
 685875-83-6P 685875-84-7P 685875-85-8P
 685875-86-9P 685875-87-0P 685875-89-2P
 685875-90-5P 685875-92-7P 685875-93-8P
 685875-94-9P 685875-98-3P 685875-99-4P

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685876-00-0P 685876-01-1P 685876-02-2P,

N-(3,5-Dichloropyridin-4-yl)-4-difluoromethoxy-8-(2-oxopyrrolidin-1-yl)dibenzofuran-1-carboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

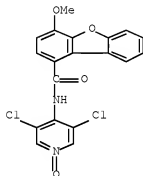
THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(preparation of dibenzofuran/dibenzothiophene derivs. useful for treatment of inflammatory and allergic disorders)

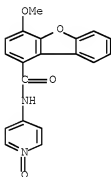
RN 685874-43-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 685874-45-7 ZCAPLUS

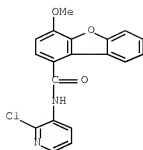
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-46-8 ZCAPLUS

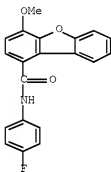
CN 1-Dibenzofurancarboxamide, N-(2-chloro-3-pyridinyl)-4-methoxy- (CA INDEX NAME)

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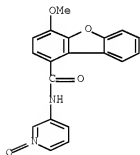
RN 685874-47-9 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(4-fluorophenyl)-4-methoxy- (CA INDEX NAME)



RN 685874-49-1 ZCAPLUS

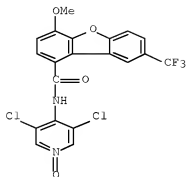
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(1-oxido-3-pyridinyl)- (CA INDEX NAME)



RN 685874-51-5 ZCAPLUS

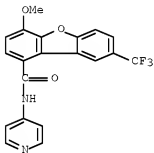
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-methoxy-8-(trifluoromethyl)- (CA INDEX NAME)

10/524815



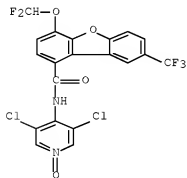
RN 685874-52-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-N-4-pyridinyl-8-(trifluoromethyl)-
(CA INDEX NAME)



RN 685874-54-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-(difluoromethoxy)-8-(trifluoromethyl)- (CA INDEX NAME)

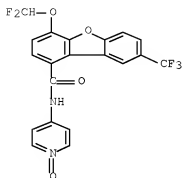


RN 685874-56-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-4-pyridinyl)-8-

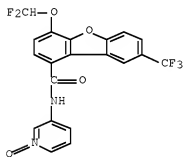
10/524815

(trifluoromethyl)- (CA INDEX NAME)



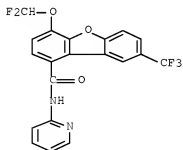
RN 685874-58-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-3-pyridinyl)-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-59-3 ZCAPLUS

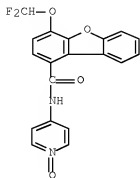
CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-2-pyridinyl-8-(trifluoromethyl)- (CA INDEX NAME)



RN 685874-62-8 ZCAPLUS

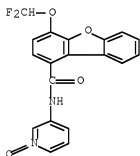
10/524815

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-4-pyridinyl)-
(CA INDEX NAME)



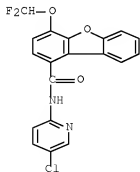
RN 685874-64-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(difluoromethoxy)-N-(1-oxido-3-pyridinyl)-
(CA INDEX NAME)



RN 685874-65-1 ZCAPLUS

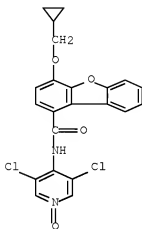
CN 1-Dibenzofurancarboxamide, N-(5-chloro-2-pyridinyl)-4-(difluoromethoxy)-
(CA INDEX NAME)



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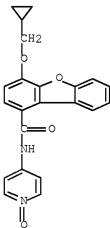
RN 685874-67-3 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(3,5-dichloro-1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-69-5 ZCAPLUS

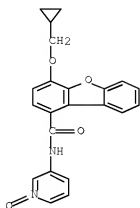
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



RN 685874-71-9 ZCAPLUS

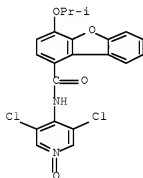
CN 1-Dibenzofurancarboxamide, 4-(cyclopropylmethoxy)-N-(1-oxido-3-pyridinyl)- (CA INDEX NAME)

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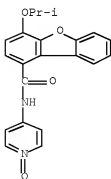
RN 685874-73-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-(1-methylethoxy)- (CA INDEX NAME)



RN 685874-75-3 ZCAPLUS

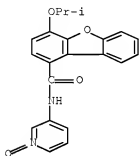
CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-(1-oxido-4-pyridinyl)- (CA INDEX NAME)



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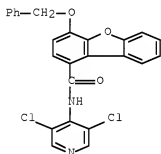
RN 685874-77-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(1-methylethoxy)-N-(1-oxido-3-pyridinyl)-
(CA INDEX NAME)



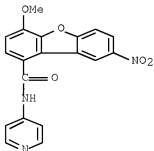
RN 685874-78-6 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-(phenylmethoxy)-
(CA INDEX NAME)



RN 685874-80-0 ZCAPLUS

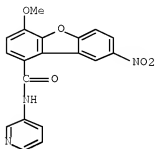
CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-4-pyridinyl- (CA INDEX
NAME)



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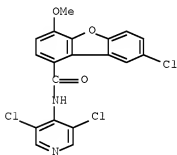
RN 685874-81-1 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-methoxy-8-nitro-N-3-pyridinyl- (CA INDEX NAME)



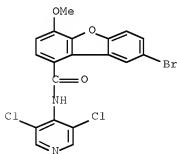
RN 685874-82-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-chloro-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



RN 685874-83-3 ZCAPLUS

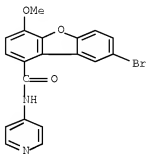
CN 1-Dibenzofurancarboxamide, 8-bromo-N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA INDEX NAME)



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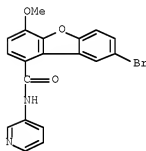
RN 685874-84-4 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-bromo-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



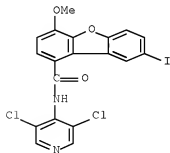
RN 685874-85-5 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-bromo-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 685874-86-6 ZCAPLUS

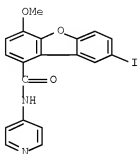
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-8-iodo-4-methoxy- (CA INDEX NAME)



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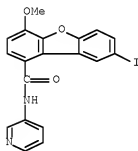
RN 685874-87-7 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-iodo-4-methoxy-N-4-pyridinyl- (CA INDEX NAME)



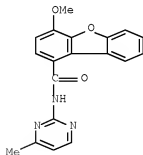
RN 685874-88-8 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-iodo-4-methoxy-N-3-pyridinyl- (CA INDEX NAME)



RN 685874-89-9 ZCAPLUS

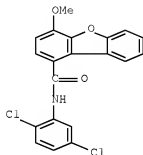
CN 1-Dibenzofurancarboxamide, 4-methoxy-N-(4-methyl-2-pyrimidinyl)- (CA INDEX NAME)



RN 685874-90-2 ZCAPLUS

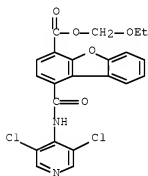
10/524815

CN 1-Dibenzofurancarboxamide, N-(2,5-dichlorophenyl)-4-methoxy- (CA INDEX NAME)



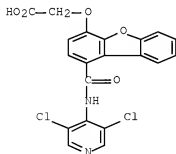
RN 685874-91-3 ZCAPLUS

CN 4-Dibenzofurancarboxylic acid, 1-[[[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-, ethoxymethyl ester (CA INDEX NAME)



RN 685874-92-4 ZCAPLUS

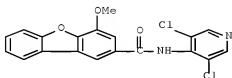
CN Acetic acid, 2-[[[1-[(3,5-dichloro-4-pyridinyl)amino]carbonyl]-4-dibenzofuranyl]oxy]- (CA INDEX NAME)



RN 685874-93-5 ZCAPLUS

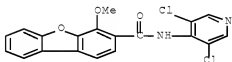
10/524815

CN 2-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA
INDEX NAME)



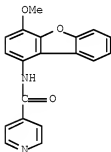
RN 685874-94-6 ZCAPLUS

CN 3-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA
INDEX NAME)



RN 685874-95-7 ZCAPLUS

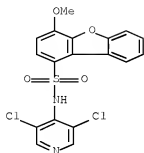
CN 4-Pyridinecarboxamide, N-(4-methoxy-1-dibenzofuranyl)- (CA INDEX NAME)



RN 685874-96-8 ZCAPLUS

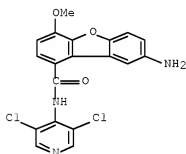
CN 1-Dibenzofuransulfonamide, N-(3,5-dichloro-4-pyridinyl)-4-methoxy- (CA
INDEX NAME)

10/524815



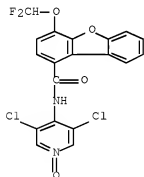
RN 685874-98-0 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 8-amino-N-(3,5-dichloro-4-pyridinyl)-4-methoxy-
(CA INDEX NAME)



RN 685874-99-1 ZCAPLUS

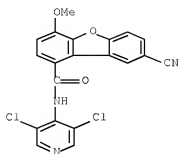
CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-1-oxido-4-pyridinyl)-4-
(difluoromethoxy)- (CA INDEX NAME)



RN 685875-00-7 ZCAPLUS

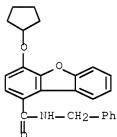
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(CA INDEX NAME)

10/524815



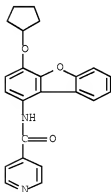
RN 685875-05-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, 4-(cyclopentyloxy)-N-(phenylmethyl)- (CA INDEX NAME)



RN 685875-06-3 ZCAPLUS

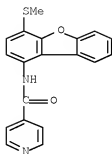
CN 4-Pyridinecarboxamide, N-[4-(cyclopentyloxy)-1-dibenzofuranyl]- (CA INDEX NAME)



RN 685875-08-5 ZCAPLUS

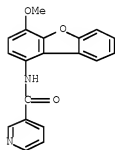
CN 4-Pyridinecarboxamide, N-[4-(methylthio)-1-dibenzofuranyl]- (CA INDEX NAME)

10/524815



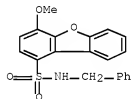
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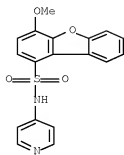
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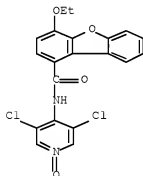
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10/524815



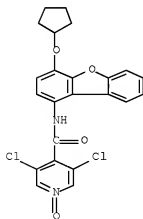
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RN 685875-13-2 ZCAPLUS

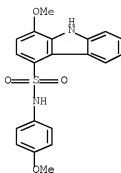
CN 4-Pyridinecarboxamide, 3,5-dichloro-N-[4-(cyclopentyloxy)-1-dibenzofuranyl]-, 1-oxide (CA INDEX NAME)



10/524815

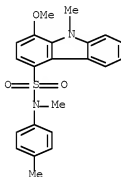
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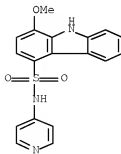
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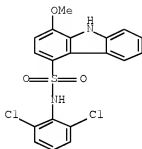
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10/524815

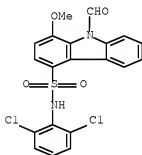
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CN 9H-Carbazole-4-sulfonamide, N-(2,6-dichlorophenyl)-1-methoxy- (CA INDEX NAME)



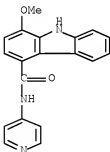
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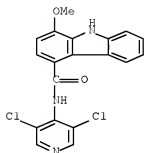
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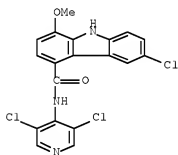
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CN 9H-Carbazole-4-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



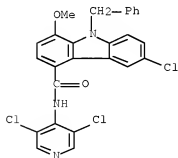
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CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-30-3 ZCAPLUS

CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-methoxy-9-(phenylmethyl)- (CA INDEX NAME)

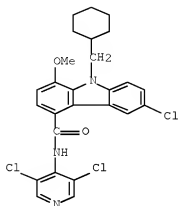


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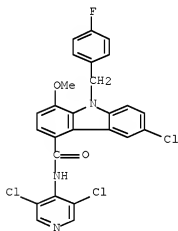
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4-pyridinyl)-1-methoxy- (CA INDEX NAME)



RN 685875-34-7 ZCAPLUS

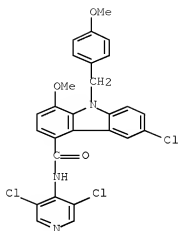
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RN 685875-36-9 ZCAPLUS

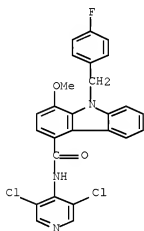
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10/524815



RN 685875-38-1 ZCAPLUS

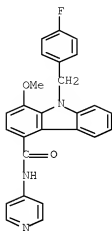
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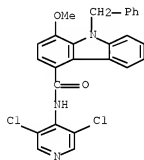
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10/524815



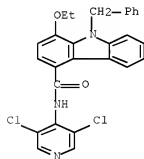
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RN 685875-48-3 ZCAPLUS

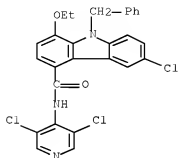
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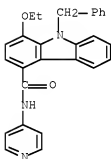
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CN 9H-Carbazole-4-carboxamide, 6-chloro-N-(3,5-dichloro-4-pyridinyl)-1-ethoxy-
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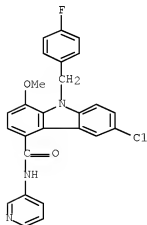
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RN 685875-57-4 ZCAPLUS

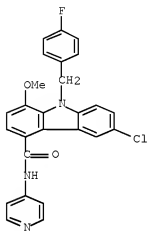
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N-3-pyridinyl- (CA INDEX NAME)



10/524815

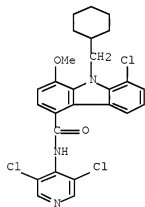
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RN 685875-59-6 ZCAPLUS

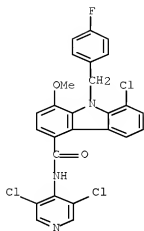
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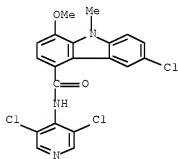
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10/524815



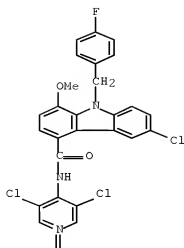
RN 685875-67-6 ZCAPLUS

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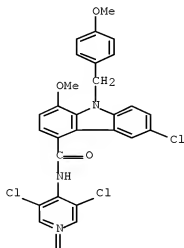
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RN 685875-72-3 ZCAPLUS

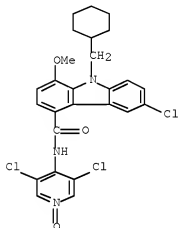
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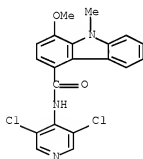
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RN 685875-74-5 ZCAPLUS

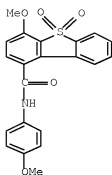
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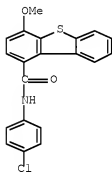
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10/524815



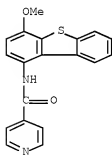
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RN 685875-83-6 ZCAPLUS

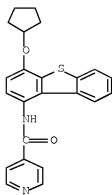
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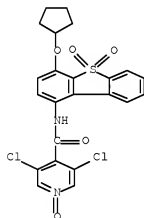
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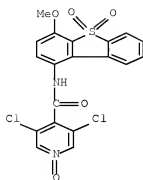
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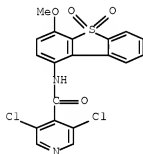
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10/524815



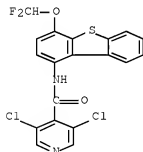
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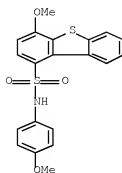
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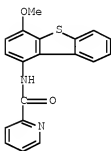
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10/524815



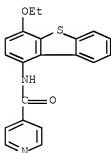
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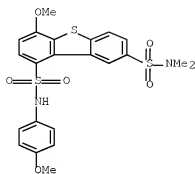
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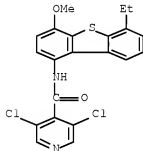
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10/524815



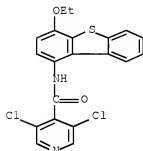
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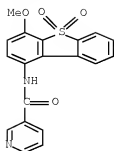
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RN 685876-00-0 ZCAPLUS

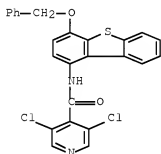
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INDEX NAME)

10/524815



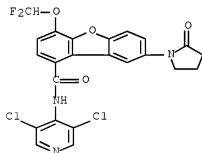
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RN 685876-02-2 ZCAPLUS

CN 1-Dibenzofurancarboxamide, N-(3,5-dichloro-4-pyridinyl)-4-
(difluoromethoxy)-8-(2-oxo-1-pyrrolidinyl)- (CA INDEX NAME)



OS.CITING REF COUNT: 11

THERE ARE 11 CAPLUS RECORDS THAT CITE THIS
RECORD (12 CITINGS)

REFERENCE COUNT: 4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
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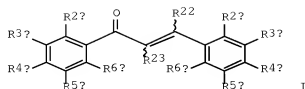
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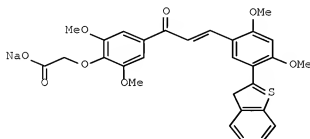
ACCESSION NUMBER: 2001:935594 ZCAPLUS Full-text
 DOCUMENT NUMBER: 136:69730
 TITLE: Preparation of
 1,3-bis-(substituted-phenyl)-2-propen-1-ones as VCAM-1
 inhibitors for treatment of inflammatory disorders
 INVENTOR(S): Meng, Charles Q.; Ni, Liming; Sikorski, James A.;
 Hoong, Lee K.
 PATENT ASSIGNEE(S): Atherogenics, Inc., USA
 SOURCE: PCT Int. Appl., 220 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098291	A2	20011227	WO 2001-US19720	20010620 <--
WO 2001098291	A3	20020516		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2413878	A1	20011227	CA 2001-2413878	20010620 <--
BR 2001011889	A	20030624	BR 2001-11889	20010620 <--
EP 1330448	A2	20030730	EP 2001-946583	20010620 <--
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 6608101	B1	20030819	US 2001-886348	20010620 <--
JP 2004501147	T	20040115	JP 2002-504247	20010620 <--
NZ 523443	A	20041126	NZ 2001-523443	20010620 <--
MX 2002012660	A	20040514	MX 2002-12660	20021218 <--
IN 2003DN00008	A	20060609	IN 2003-DN8	20030101 <--
ZA 2003000134	A	20051006	ZA 2003-134	20030106 <--
US 20030236298	A1	20031225	US 2003-443470	20030521 <--
US 7078431	B2	20060718		
ZA 2005003708	A	20070425	ZA 2005-3708	20050509 <--
US 20060258735	A1	20061116	US 2006-485940	20060713 <--
PRIORITY APPLN. INFO.:			US 2000-212769P	P 20000620 <--
			US 2000-255934P	P 20001215 <--
			US 2001-886348	A1 20010620 <--
			WO 2001-US19720	W 20010620 <--
			US 2003-443470	A1 20030521 <--

OTHER SOURCE(S): MARPAT 136:69730
 GI



I



II

AB Title compds. I [wherein R2a, R3a, R4a, R5a, R6a, R2b, R3b, R4b, R5b, and R6b = independently H, (cyclo)alkyl, (hetero)aryl, carbocyclyl, (halo)alkylthio, (un)substituted alkoxy or amino, (halo)acyl, amido, (halo)alkylsulfonyl, aminocarbonyl, alkenyl, alkynyl, halo, OH, SH, CN, NO2, SO3H, sulf(on)amido, PO3H2, alditol, carbohydrate, amino acid, etc.; R22 and R23 = independently H or alkyl; or R22 and R6a or R23 and R6a can join together to form a bridged carbocycle, (hetero)aryl, or heterocycle; R2a and R3a, R3a and R4a, R4a and R5a, R5a and R6a, R2b and R3b, R3b and R4b, R4b and R5b, or R5b and R6b and independently join to form a bridged (un)substituted carbocycle, cycloalkenyl, cycloalk(en)ylcarbonyl, (hetero)aryl, heterocycle, or alkylenedioxy; and the E or Z isomers thereof] were prepared to inhibit the expression of VCAM-1. For example, 3',5'-dimethoxy-4'-hydroxyacetophenone was treated with Et glycolate, PPh3, and di-Et azodicarboxylate in THF to give 4'-ethoxycarbonylmethoxy-3',5'-dimethoxyacetophenone (90%). Coupling the acetophenone and 5-(benzo[b]thien-2-yl)-2,4-dimethoxybenzaldehyde (preparation given) in the presence of NaOH in absolute EtOH afforded the 1,3-diphenyl-2-propen-1-one II (39%), which stimulated cultured human aortic smooth muscle cell activity with IC50 of 0.45 μ M. I are useful for the treatment of inflammatory disorders that are mediated by VCAM-1, including arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

IC ICM C07D333-00

CC 27-8 (Heterocyclic Compounds (One Hetero Atom))

Section cross-reference(s): 1

IT Cystic fibrosis

Dermatitis

Graves' disease

Psoriasis

Transplant rejection

(treatment; preparation of bis(substituted phenyl)propenones as VCAM-1 inhibitors for treatment of inflammatory disorders)

IT Antidepressants

(tricyclic; co-administration of bis(substituted

phenyl)propenone VCAM-1 inhibitors with other biol. agents)

IT 60-87-7, Promethazine 68-88-2, Hydroxyzine 82-88-2
 , Phenindamine 82-92-8, Marezine 86-22-6, Brompheniramine 91-84-9,
 Pyrilamine 113-92-8, Chlorthimeton 147-24-0, Benadryl 550-70-9,
 Actidil 969-33-5, Periactin 1229-35-2, Tacaryl
 2438-32-6, Polaramine 4330-99-8, Temaril 8064-07-1, Antivert
 14976-57-9, Tavist 50679-08-8, Seldane 68844-77-9, Hismanal
 79794-75-5, Claritin 153439-40-8, Allegra
 RL: PAC (Pharmacological activity); TRU (Therapeutic
 use); BIOL (Biological study); USES (Uses)
 (co-administration of bis(substituted phenyl)propenone VCAM-1
 inhibitors with antihistamines)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone
 acetate 50-04-4, Cortisone Acetate 50-23-7,
 Hydrocortisone 50-24-8, Prednisolone 52-21-1,
 Prednisolone Acetate 52-39-1, Aldosterone 53-03-2,
 Prednisone 53-34-9, Fluprednisolone 53-36-1,
 Methylprednisolone Acetate 56-47-3, Deoxycortone Acetate
 67-73-2, Fluocinolone Acetonide 67-78-7, Triamcinolone
 Diacetate 76-25-5, Azmacort 79-61-8, Dichlorisone
 Acetate 83-43-2, Methylprednisolone 124-94-7,
 Triamcinolone 125-02-0, Prednisolone Sodium Phosphate
 125-03-1, Hydrocortamate Hydrochloride 125-04-2,
 Hydrocortisone Sodium Succinate 125-10-0, Prednisone Acetate
 151-73-5, Betamethasone Sodium Phosphate 152-97-6,
 Fluocortolone 303-40-2, Fluocortolone Hexanoate
 312-93-6, Dexamethasone Phosphate 356-12-7,
 Fluocinonide 378-44-9, Betamethasone 382-67-2,
 Desoxymethasone 426-13-1, Fluorometholone 508-99-6
 , Hydrocortisone Cypionate 514-36-3, Fludrocortisone Acetate
 599-33-7, Prednylidene 630-67-1 638-94-8,
 Desonide 806-48-0, Deoxycortone Pivalate 987-24-6,
 Betamethasone Acetate 1107-99-9, Prednisolone Pivalate
 1110-40-3, Cortivazol 1177-87-3, Dexamethasone Acetate
 1247-42-3, Meprednisone 1255-35-2, Fluprednidene
 Acetate 1524-88-5, Flurandrenolone 1597-82-6,
 Paramethasone Acetate 1715-33-9, Prednisolone Sodium Succinate
 2002-29-1, Flumethasone Pivalate 2135-17-3,
 Flumethasone 2152-44-5, Betamethasone Valerate
 2203-97-6, Hydrocortisone Hemisuccinate 2265-64-7,
 Dexamethasone Isonicotinate 2375-03-3, Methylprednisolone
 Sodium Succinate 2392-39-4, Dexamethasone Sodium Phosphate
 2668-66-8, Medrysone 2825-60-7, Formocortol
 2920-86-7, Prednisolone Hemisuccinate 2921-57-5,
 Methylprednisolone Hemisuccinate 3093-35-4, Halcinonide
 3385-03-3, Flunisolide 3693-39-8, Fluclorolone
 Acetonide 3801-06-7, Fluorometholone Acetate
 3936-02-5 5060-55-9, Prednisolone steaglate
 5251-34-3, Cloprednol 5534-09-8, Vanceryl
 5593-20-4, Betamethasone Dipropionate 5611-51-8,
 Triamcinolone Hexacetone 6000-74-4, Hydrocortisone Sodium
 Phosphate 7681-14-3, Prednisolone Tebutate
 13609-67-1, Hydrocortisone Butyrate 14484-47-0,
 Deflazacort 19888-56-3, Fluazacort 20423-99-8,
 Deprodone 22298-29-9, Betamethasone Benzoate
 23674-86-4, Difluprednate 25122-46-7, Clobetasol
 Propionate 25122-57-0, Clobetasone Butyrate
 29205-06-9, Fluocortolone Pivalate 33564-31-7,
 Diflorasone Diacetate 34097-16-0, Clolocortolone Pivalate
 35100-44-8, Endrysone 41767-29-7, Fluocortin Butyl

49697-38-3, Rimexolone 59629-82-8, Halometasone
 51022-69-6, Amcinonide 51333-22-3, Pulmicort
 53716-43-1, Bendacort 55560-96-8, Tixocortol Pivalate
 57524-89-7, Hydrocortisone Valerate 58497-00-0,
 Procinnonide 58524-83-7, Ciprocinonide 59198-70-8,
 Diflucortolone Valerate 66734-13-2, Alclometasone Dipropionate
 66852-54-8, Halobetasol Propionate 66877-67-6,
 Domoprednate 69164-69-8 73771-64-7, Prednicarbate
 77326-96-6, Aerobid M 80474-14-2, Flovent
 83919-23-7, Mometasone Furoate 86022-88-0,
 Cyclomethasone

RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1
 inhibitors with corticosteroids)

IT 51-55-8, Atropine, biological studies 54-31-9, Frusemide 58-55-9,
 Theophylline, biological studies 59-05-2, Methotrexate 69-89-6D,
 Xanthine, derivs. 317-34-0, Aminophylline 2751-09-9, Troleandomycin
 4499-40-5, Choleleryl, biological studies 9003-98-9, DNAase 9005-49-6,
 Heparin, biological studies 12244-57-4, Myochrysine 15826-37-6, Sodium
 cromoglycate 21829-25-4, Nifedipine 22254-24-6, Atrovent
 30286-75-0, Oxitropium bromide 34580-13-7, Ketotifen
 59865-13-3, Cyclosporin 66357-35-5, Ranitidine 69049-74-7,
 Tilade 94470-67-4, Cromakalim 101975-10-4, Zardaverine
 104987-11-3, FK-506 107753-78-6, Accolate 111406-87-2,
 Zileuton

RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1
 inhibitors with other biol. agents)

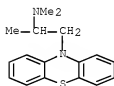
IT 60-87-7, Promethazine 82-88-2, Phenindamine
 969-33-5, Periactin 1229-35-2, Tacaryl
 4330-99-8, Temaril 79794-75-5, Claritin

RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1
 inhibitors with antihistamines)

RN 60-87-7 ZCAPLUS

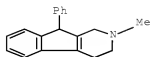
CN 10H-Phenothiazine-10-ethanamine, N,N, α -trimethyl- (CA INDEX NAME)



RN 82-88-2 ZCAPLUS

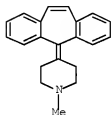
CN 1H-Indeno[2,1-c]pyridine, 2,3,4,9-tetrahydro-2-methyl-9-phenyl- (CA INDEX NAME)

10/524815



RN 969-33-5 ZCAPLUS

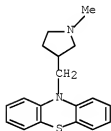
CN Piperidine, 4-(5H-dibenzo[a,d]cyclohept-5-ylidene)-1-methyl-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 1229-35-2 ZCAPLUS

CN 10H-Phenothiazine-10-[(1-methyl-3-pyrrolidinyl)methyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 4330-99-8 ZCAPLUS

CN 10H-Phenothiazine-10-propanamine, N,N,β-trimethyl-, (2R,3R)-2,3-dihydroxybutanedioate (2:1) (CA INDEX NAME)

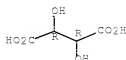
CM 1

CRN 87-69-4

CMF C4 H6 O6

Absolute stereochemistry.

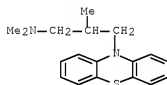
10/524815



CM 2

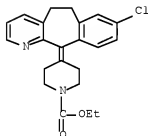
CRN 84-96-8

CMF C18 H22 N2 S



RN 79794-75-5 ZCAPLUS

CN 1-Piperidinecarboxylic acid, 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-, ethyl ester (CA INDEX NAME)



IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone acetate 50-04-4, Cortisone Acetate 50-23-7, Hydrocortisone 50-24-8, Prednisolone 52-21-1, Prednisolone Acetate 52-39-1, Aldosterone 53-03-2, Prednisone 53-34-9, Fluprednisolone 53-36-1, Methylprednisolone Acetate 56-47-3, Deoxycortone Acetate 67-73-2, Fluocinolone Acetonide 67-78-7, Triamcinolone Diacetate 76-25-5, Azmacort 79-61-8, Dichlorisone Acetate 83-43-2, Methylprednisolone 124-94-7, Triamcinolone 125-02-0, Prednisolone Sodium Phosphate 125-03-1, Hydrocortamate Hydrochloride 125-04-2, Hydrocortisone Sodium Succinate 125-10-0, Prednisone Acetate 151-73-5, Betamethasone Sodium Phosphate 152-97-6, Fluocortolone 303-40-2, Fluocortolone Hexanoate

312-93-6, Dexamethasone Phosphate 356-12-7,
 Fluciclonide 378-44-9, Betamethasone 382-67-2,
 Desoxymethasone 426-13-1, Fluorometholone 508-99-6
 , Hydrocortisone Cypionate 514-36-3, Fludrocortisone Acetate
 599-33-7, Prednylidene 630-67-1 638-94-8,
 Desonide 808-48-0, Deoxycortone Pivalate 987-24-6,
 Betamethasone Acetate 1107-99-9, Prednisolone Pivalate
 1110-40-3, Cortivazol 1177-87-3, Dexamethasone Acetate
 1247-42-3, Meprednisone 1255-35-2, Fluprednidene
 Acetate 1524-88-5, Flurandrenolone 1597-82-6,
 Paramethasone Acetate 1715-33-9, Prednisolone Sodium Succinate
 2002-29-1, Flumethasone Pivalate 2135-17-3,
 Flumethasone 2152-44-5, Betamethasone Valerate
 2203-97-6, Hydrocortisone Hemisuccinate 2265-64-7,
 Dexamethasone Isonicotinate 2375-03-3, Methylprednisolone
 Sodium Succinate 2392-39-4, Dexamethasone Sodium Phosphate
 2668-66-8, Medrysone 2825-60-7, Formocortol
 2920-86-7, Prednisolone Hemisuccinate 2921-57-5,
 Methylprednisolone Hemisuccinate 3093-35-4, Halcinonide
 3385-03-3, Flunisolide 3693-39-8, Fluclorolone
 Acetonide 3801-06-7, Fluorometholone Acetate
 3936-02-5 5060-55-9, Prednisolone Stearate
 5251-34-3, Cloprednol 5534-09-8, Vanceryl
 5593-20-4, Betamethasone Dipropionate 5611-51-8,
 Triamcinolone Hexacetonide 6000-74-4, Hydrocortisone Sodium
 Phosphate 7681-14-3, Prednisolone Tebutate
 13609-67-1, Hydrocortisone Butyrate 14484-47-0,
 Deflazacort 19888-56-3, Fluzacort 20423-99-8,
 Deprodone 22298-29-9, Betamethasone Benzoate
 23674-86-4, Difluprednate 25122-46-7, Clobetasol
 Propionate 25122-57-0, Clobetasone Butyrate
 29205-06-9, Fluocortolone Pivalate 33564-31-7,
 Diflorasone Diacetate 34097-16-0, Clocortolone Pivalate
 35100-44-8, Endrysone 41767-29-7, Fluocortin Butyl
 49697-38-3, Rimexolone 50629-82-8, Halometasone
 51022-69-6, Amcinonide 51333-22-3, Pulmicort
 53716-43-1, Bendacort 55560-96-8, Tixocortol Pivalate
 57524-89-7, Hydrocortisone Valerate 58497-00-0,
 Procinonide 58524-83-7, Ciprocinonide 59198-70-8,
 Diflucortolone Valerate 66734-13-2, Alclometasone Dipropionate
 66852-54-8, Halobetasol Propionate 66877-67-6,
 Domoprednate 69164-69-8 73771-04-7, Prednicarbate
 77326-96-6, Aerobid M 80474-14-2, Flovent
 83919-23-7, Mometasone Furoate 86022-88-0,
 Cyclomethasone

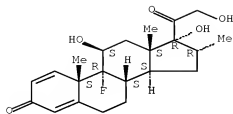
RL: PAC (Pharmacological activity); THU (Therapeutic
 use); BIOL (Biological study); USES (Uses)
 (co-administration of bis(substituted phenyl)propenone VCAM-1
 inhibitors with corticosteroids)

RN 50-02-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-,
 (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

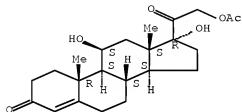
10/524815



RN 50-03-3 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-, (11β)- (CA INDEX NAME)

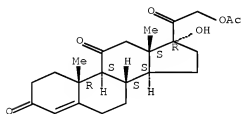
Absolute stereochemistry.



RN 50-04-4 ZCAPLUS

CN Pregn-4-ene-3,11,20-trione, 21-(acetyloxy)-17-hydroxy-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

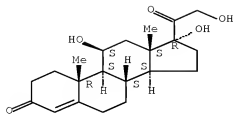


RN 50-23-7 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11β)- (CA INDEX NAME)

Absolute stereochemistry.

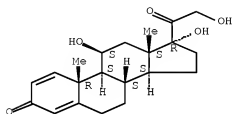
10/524815



RN 50-24-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-, (11 β)- (CA INDEX NAME)

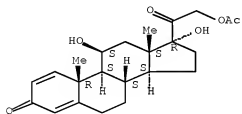
Absolute stereochemistry.



RN 52-21-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry.

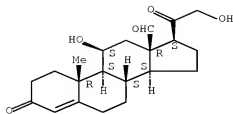


RN 52-39-1 ZCAPLUS

CN Pregn-4-en-18-al, 11,21-dihydroxy-3,20-dioxo-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry.

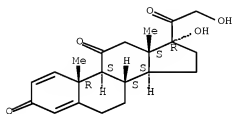
10/524815



RN 53-03-2 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy- (CA INDEX NAME)

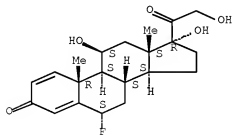
Absolute stereochemistry.



RN 53-34-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,17,21-trihydroxy-,
(6 α ,11 β)- (CA INDEX NAME)

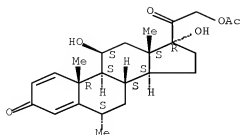
Absolute stereochemistry.



RN 53-36-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-11,17-dihydroxy-6-methyl-,
(6 α ,11 β)- (CA INDEX NAME)

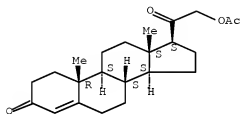
Absolute stereochemistry.



RN 56-47-3 ZCAPLUS

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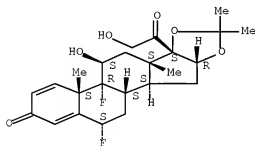
Absolute stereochemistry.



RN 67-73-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

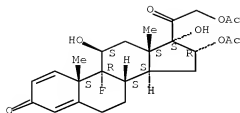


RN 67-78-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 16,21-bis(acetyloxy)-9-fluoro-11,17-dihydroxy-, (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

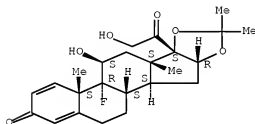
10/524815



RN 76-25-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11β,16α)- (CA INDEX NAME)

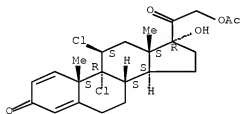
Absolute stereochemistry.



RN 79-61-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9,11-dichloro-17-hydroxy-, (11β)- (CA INDEX NAME)

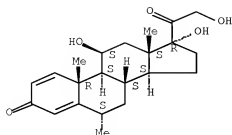
Absolute stereochemistry.



RN 83-43-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-6-methyl-, (6α,11β)- (CA INDEX NAME)

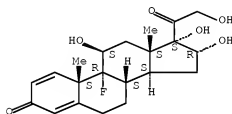
Absolute stereochemistry.



RN 124-94-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,16,17,21-tetrahydroxy-,
(11 β ,16 α)- (CA INDEX NAME)

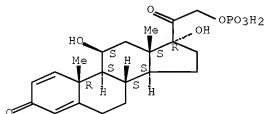
Absolute stereochemistry.



RN 125-02-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-(phosphonoxy)-, disodium
salt, (11 β)- (CA INDEX NAME)

Absolute stereochemistry.



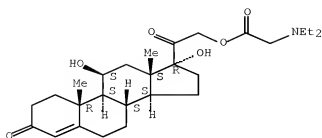
● 2 Na

RN 125-03-1 ZCAPLUS

CN Glycine, N,N-diethyl-, (11 β)-11,17-dihydroxy-3,20-dioxopregn-4-en-21-
yl ester, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/524815

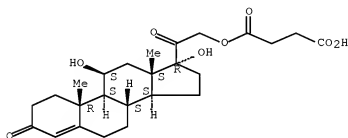


● HCl

RN 125-04-2 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, sodium salt (1:1), (11 β)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

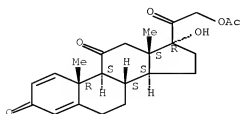


● Na

RN 125-10-0 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 21-(acetyloxy)-17-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.



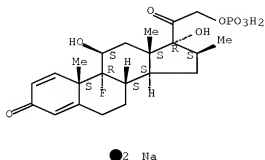
RN 151-73-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-

10/524815

(phosphonoxy)-, sodium salt (1:2), (11 β ,16 β)- (CA INDEX NAME)

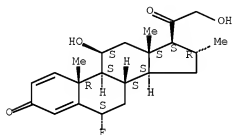
Absolute stereochemistry.



RN 152-97-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

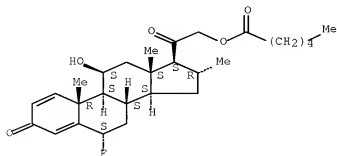
Absolute stereochemistry.



RN 303-40-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11-hydroxy-16-methyl-21-[(1-oxohexyl)oxy]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

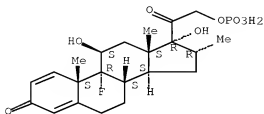


RN 312-93-6 ZCAPLUS

10/524815

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonoxy)-, (11 β ,16 α)- (CA INDEX NAME)

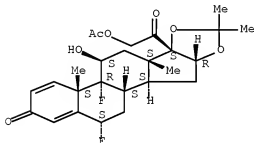
Absolute stereochemistry.



RN 356-12-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

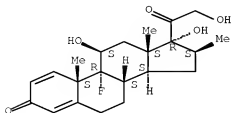
Absolute stereochemistry.



RN 378-44-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17,21-trihydroxy-16-methyl-, (11 β ,16 β)- (CA INDEX NAME)

Absolute stereochemistry.



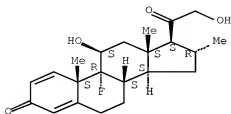
RN 382-67-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-,

10/524815

(11 β ,16 α)- (CA INDEX NAME)

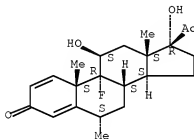
Absolute stereochemistry.



RN 426-13-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-6-methyl-,
(6 α ,11 β)- (CA INDEX NAME)

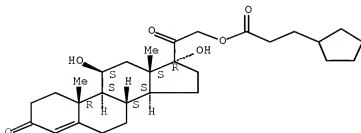
Absolute stereochemistry.



RN 508-99-6 ZCAPLUS

CN Pregna-4-ene-3,20-dione, 21-(3-cyclopentyl-1-oxopropoxy)-11,17-dihydroxy-,
(11 β)- (CA INDEX NAME)

Absolute stereochemistry.

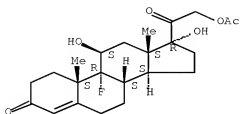


RN 514-36-3 ZCAPLUS

CN Pregna-4-ene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-,
(11 β)- (CA INDEX NAME)

10/524815

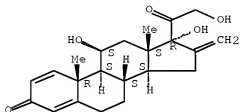
Absolute stereochemistry.



RN 599-33-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17,21-trihydroxy-16-methylene-, (11β)- (CA INDEX NAME)

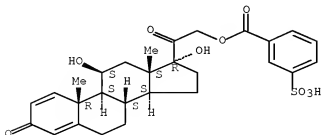
Absolute stereochemistry.



RN 630-67-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(3-sulfobenzoyl)oxy]-, sodium salt (1:1), (11β)- (CA INDEX NAME)

Absolute stereochemistry.



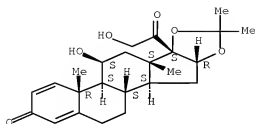
● Na

RN 638-94-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11β,16α)- (CA INDEX NAME)

10/524815

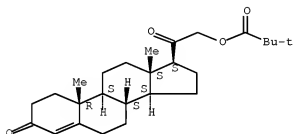
Absolute stereochemistry.



RN 808-48-0 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)- (CA INDEX NAME)

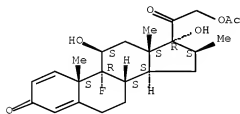
Absolute stereochemistry.



RN 987-24-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methyl-, (11 β ,16 β)- (CA INDEX NAME)

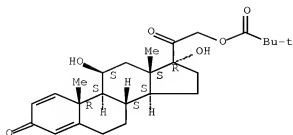
Absolute stereochemistry.



RN 1107-99-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

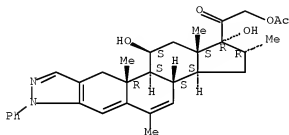
Absolute stereochemistry.



RN 1110-40-3 ZCAPLUS

CN 2'-H-Pregna-2,4,6-trieno[3,2-c]pyrazol-20-one,
21-(acetyloxy)-11,17-dihydroxy-6,16-dimethyl-2'-phenyl-,
(11 β ,16 α)- (CA INDEX NAME)

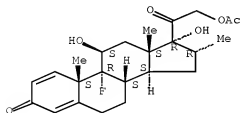
Absolute stereochemistry.



RN 1177-87-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-
methyl-, (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

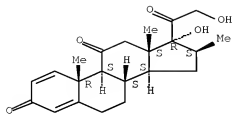


RN 1247-42-3 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 17,21-dihydroxy-16-methyl-, (16 β)-
(CA INDEX NAME)

Absolute stereochemistry.

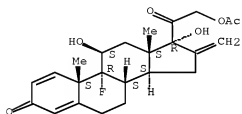
10/524815



RN 1255-35-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methylene-, (11 β)- (CA INDEX NAME)

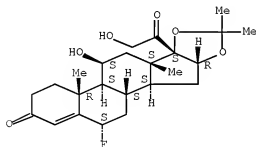
Absolute stereochemistry.



RN 1524-88-5 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

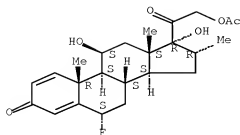


RN 1597-82-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6-fluoro-11,17-dihydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

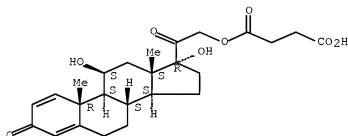
10/524815



RN 1715-33-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, monosodium salt, (11 β)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

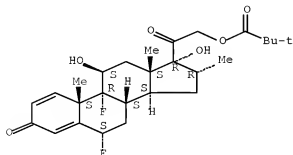


● Na

RN 2002-29-1 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-6,9-difluoro-11,17-dihydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.



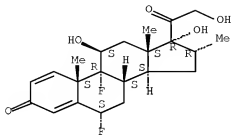
RN 2135-17-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11,17,21-trihydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

10/524815

(6 α ,11 β ,16 α)- (CA INDEX NAME)

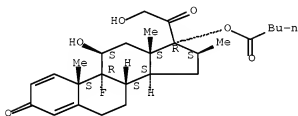
Absolute stereochemistry.



RN 2152-44-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16-methyl-17-[(1-oxopentyl)oxy]-, (11 β ,16 β)- (CA INDEX NAME)

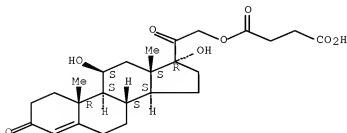
Absolute stereochemistry.



RN 2203-97-6 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

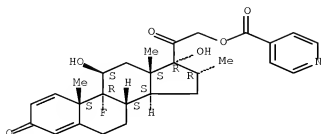


RN 2265-64-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(4-pyridinylcarbonyl)oxy]-, (11 β ,16 α)- (CA INDEX NAME)

10/524815

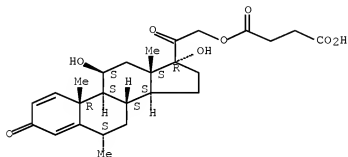
Absolute stereochemistry.



RN 2375-03-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, monosodium salt, (6 α ,11 β)- (CA INDEX NAME)

Absolute stereochemistry.

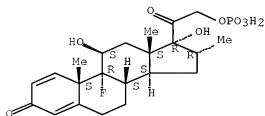


● Na

RN 2392-39-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-(phosphonoxy)-, sodium salt (1:2), (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.



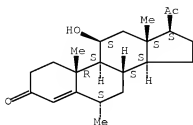
●2 Na

10/524815

RN 2668-66-8 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11-hydroxy-6-methyl-, (6 α ,11 β)- (CA INDEX NAME)

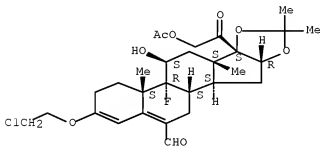
Absolute stereochemistry.



RN 2825-60-7 ZCAPLUS

CN Pregna-3,5-diene-6-carboxaldehyde, 21-(acetyloxy)-3-(2-chloroethoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-20-oxo-, (11 β ,16 α)- (CA INDEX NAME)

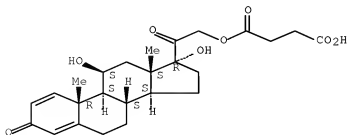
Absolute stereochemistry.



RN 2920-86-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

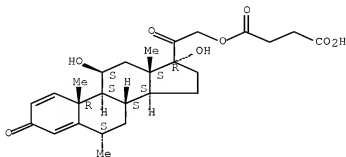


10/524815

RN 2921-57-5 ZCAPLUS

CN Pregn-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-6-methyl-, (6 α ,11 β)- (CA INDEX NAME)

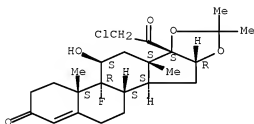
Absolute stereochemistry.



RN 3093-35-4 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-chloro-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 β ,16 α)- (CA INDEX NAME)

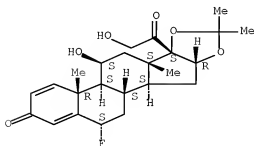
Absolute stereochemistry.



RN 3385-03-3 ZCAPLUS

CN Pregn-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

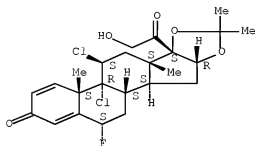


10/524815

RN 3693-39-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9,11-dichloro-6-fluoro-21-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

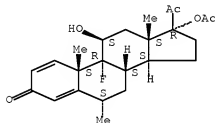
Absolute stereochemistry.



RN 3801-06-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-(acetyloxy)-9-fluoro-11-hydroxy-6-methyl-, (6 α ,11 β)- (CA INDEX NAME)

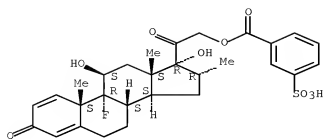
Absolute stereochemistry.



RN 3936-02-5 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11,17-dihydroxy-16-methyl-21-[(3-sulfobenzoyl)oxy]-, sodium salt (1:1) (CA INDEX NAME)

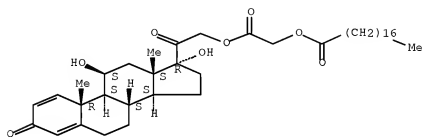
Absolute stereochemistry.



RN 5060-55-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[[[(1-oxooctadecyl)oxy]acetyl]oxy]-, (11β)- (CA INDEX NAME)

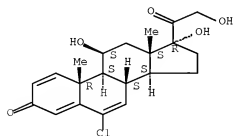
Absolute stereochemistry.



RN 5251-34-3 ZCAPLUS

CN Pregna-1,4,6-triene-3,20-dione, 6-chloro-11,17,21-trihydroxy-, (11β)- (CA INDEX NAME)

Absolute stereochemistry.

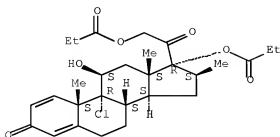


RN 5534-09-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11β,16β)- (CA INDEX NAME)

10/524815

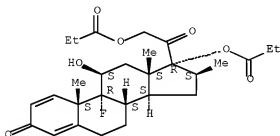
Absolute stereochemistry.



RN 5593-20-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (11 β ,16 β)- (CA INDEX NAME)

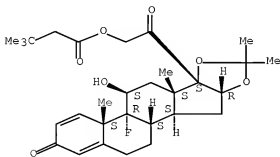
Absolute stereochemistry.



RN 5611-51-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.



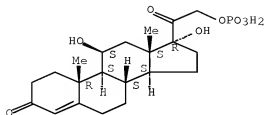
RN 6000-74-4 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-(phosphonooxy)-, sodium salt

10/524815

(1:2), (11 β)- (CA INDEX NAME)

Absolute stereochemistry.

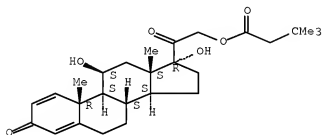


● 2 Na

RN 7681-14-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(3,3-dimethyl-1-oxobutoxy)-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

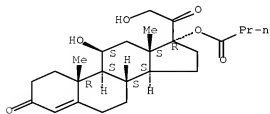
Absolute stereochemistry.



RN 13609-67-1 ZCAPLUS

CN Pregna-4-ene-3,20-dione, 11,21-dihydroxy-17-(1-oxobutoxy)-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry.



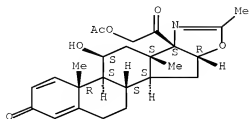
RN 14484-47-0 ZCAPLUS

CN 5'H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione, 21-(acetyloxy)-11-hydroxy-2'-methyl-, (11 β ,16 β)- (CA INDEX NAME)

10/524815

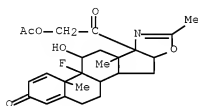
NAME)

Absolute stereochemistry.



RN 19888-56-3 ZCAPLUS

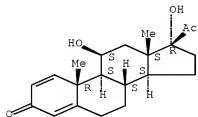
CN 5'H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione,
21-(acetyloxy)-9-fluoro-11-hydroxy-2'-methyl-, (11 β ,16 β)- (CA
INDEX NAME)



RN 20423-99-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-, (11 β)- (CA INDEX
NAME)

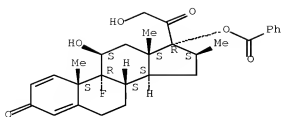
Absolute stereochemistry.



RN 22298-29-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-(benzoyloxy)-9-fluoro-11,21-dihydroxy-16-
methyl-, (11 β ,16 β)- (CA INDEX NAME)

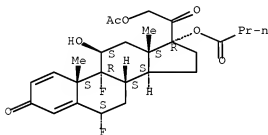
Absolute stereochemistry.



RN 23674-86-4 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-6,9-difluoro-11-hydroxy-17-(1-oxobutoxy)-, (6 α ,11 β)- (CA INDEX NAME)

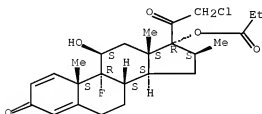
Absolute stereochemistry.



RN 25122-46-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-chloro-9-fluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (11 β ,16 β)- (CA INDEX NAME)

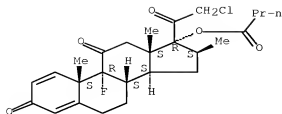
Absolute stereochemistry.



RN 25122-57-0 ZCAPLUS

CN Pregna-1,4-diene-3,11,20-trione, 21-chloro-9-fluoro-16-methyl-17-(1-oxobutoxy)-, (16 β)- (CA INDEX NAME)

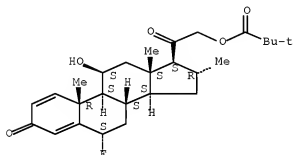
Absolute stereochemistry.



RN 29205-06-9 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(2,2-dimethyl-1-oxopropoxy)-6-fluoro-11-hydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

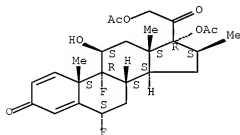
Absolute stereochemistry.



RN 33564-31-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17,21-bis(acetyloxy)-6,9-difluoro-11-hydroxy-16-methyl-, (6 α ,11 β ,16 β)- (CA INDEX NAME)

Absolute stereochemistry.

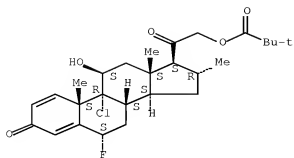


RN 34097-16-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 9-chloro-21-(2,2-dimethyl-1-oxopropoxy)-6-fluoro-11-hydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

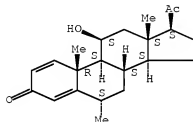
10/524815



RN 35100-44-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11-hydroxy-6-methyl-, (6 α ,11 β)-
(CA INDEX NAME)

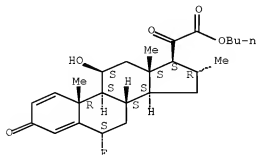
Absolute stereochemistry.



RN 41767-29-7 ZCAPLUS

CN Pregna-1,4-dien-21-oic acid, 6-fluoro-11-hydroxy-16-methyl-3,20-dioxo-,
butyl ester, (6 α ,11 β ,16 α)- (CA INDEX NAME)

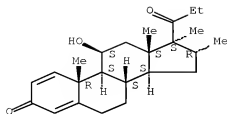
Absolute stereochemistry.



RN 49697-38-3 ZCAPLUS

CN Androsta-1,4-dien-3-one, 11-hydroxy-16,17-dimethyl-17-(1-oxopropyl)-,
(11 β ,16 α ,17 β)- (CA INDEX NAME)

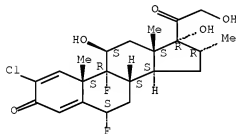
Absolute stereochemistry.



RN 50629-82-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 2-chloro-6,9-difluoro-11,17,21-trihydroxy-16-methyl-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

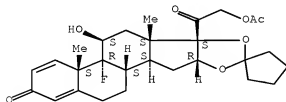
Absolute stereochemistry.



RN 51022-69-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-(acetyloxy)-16,17-[cyclopentylidenebis(oxy)]-9-fluoro-11-hydroxy-, (11 β ,16 α)- (CA INDEX NAME)

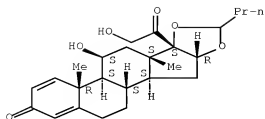
Absolute stereochemistry.



RN 51333-22-3 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 16,17-[butylidenebis(oxy)]-11,21-dihydroxy-, (11 β ,16 α)- (CA INDEX NAME)

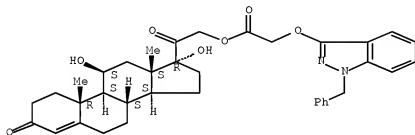
Absolute stereochemistry.



RN 53716-43-1 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17-dihydroxy-21-[[2-[[1-(phenylmethyl)-1H-indazol-3-yl]oxy]acetyl]oxy]-, (11 β)- (CA INDEX NAME)

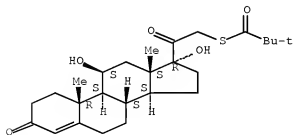
Absolute stereochemistry.



RN 55560-96-8 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 21-[(2,2-dimethyl-1-oxopropyl)thio]-11,17-dihydroxy-, (11 β)- (CA INDEX NAME)

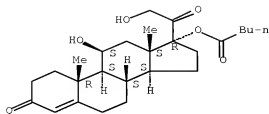
Absolute stereochemistry.



RN 57524-89-7 ZCAPLUS

CN Pregn-4-ene-3,20-dione, 11,21-dihydroxy-17-[(1-oxopentyl)oxy]-, (11 β)- (CA INDEX NAME)

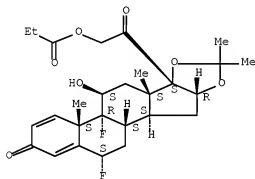
Absolute stereochemistry.



RN 58497-00-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-21-(1-oxopropoxy)-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

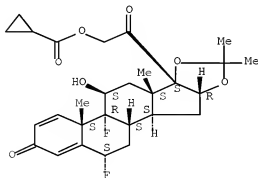
Absolute stereochemistry.



RN 58524-83-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[(cyclopropylcarbonyl)oxy]-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.

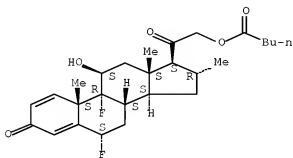


10/524815

RN 59198-70-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6,9-difluoro-11-hydroxy-16-methyl-21-[(1-oxopentyl)oxy]-, (6 α ,11 β ,16 α)- (CA INDEX NAME)

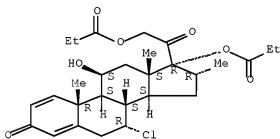
Absolute stereochemistry.



RN 66734-13-2 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 7-chloro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-, (7 α ,11 β ,16 α)- (CA INDEX NAME)

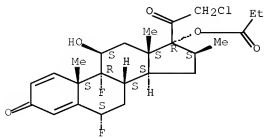
Absolute stereochemistry.



RN 66852-54-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-, (6 α ,11 β ,16 β)- (CA INDEX NAME)

Absolute stereochemistry.

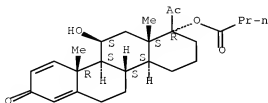


10/524815

RN 66877-67-6 ZCAPLUS

CN Butanoic acid, (1R,4aS,4bS,10aR,10bS,11S,12aS)-1-acetyl-1,2,3,4,4a,4b,5,6,8,10a,10b,11,12,12a-tetradecahydro-11-hydroxy-10a,12a-dimethyl-8-oxo-1-chrysenyl ester (CA INDEX NAME)

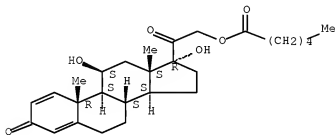
Absolute stereochemistry.



RN 69164-69-8 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 11,17-dihydroxy-21-[(1-oxohexyl)oxy]-, (11 β)- (CA INDEX NAME)

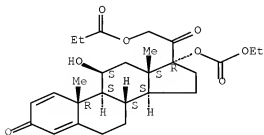
Absolute stereochemistry.



RN 73771-04-7 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 17-[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)-, (11 β)- (CA INDEX NAME)

Absolute stereochemistry.



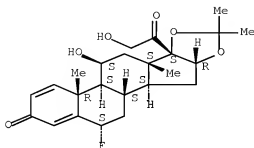
RN 77326-96-6 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 6-fluoro-11,21-dihydroxy-16,17-[(1-

10/524815

methylthylidene)bis(oxy)]-, hydrate (2:1), (6 α ,11 β ,16 α)-
(CA INDEX NAME)

Absolute stereochemistry.

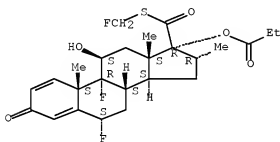


● 1/2 H₂O

RN 80474-14-2 ZCAPLUS

CN Androsta-1,4-diene-17-carbothioic acid,
6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)-,
S-(fluoromethyl) ester, (6 α ,11 β ,16 α ,17 α)- (CA
INDEX NAME)

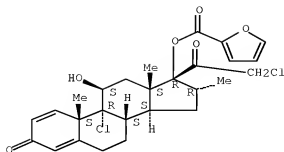
Absolute stereochemistry.



RN 83919-23-7 ZCAPLUS

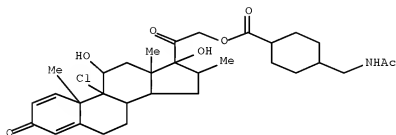
CN Pregna-1,4-diene-3,20-dione, 9,21-dichloro-17-[(2-furanylcarbonyl)oxy]-11-
hydroxy-16-methyl-, (11 β ,16 α)- (CA INDEX NAME)

Absolute stereochemistry.



RN 86022-88-0 ZCAPLUS

CN Pregna-1,4-diene-3,20-dione, 21-[[[trans-4-
[(acetylamino)methyl]cyclohexyl]carbonyl]oxy]-9-chloro-11,17-dihydroxy-16-
methyl-, (11 β ,16 β)- (CA INDEX NAME)



IT 30286-75-0, Oxitropium bromide 34580-13-7, Ketotifen

69049-74-7, Tilade 104987-11-3, FK-506

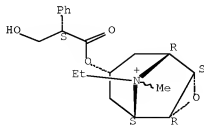
RL: PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)

(co-administration of bis(substituted phenyl)propenone VCAM-1
inhibitors with other biol. agents)

RN 30286-75-0 ZCAPLUS

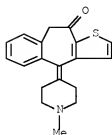
CN 3-Oxa-9-azoniatricyclo[3.3.1.0^{2,4}]nonane,
9-ethyl-7-[(2S)-3-hydroxy-1-oxo-2-phenylpropoxy]-9-methyl-, bromide (1:1),
(1 α ,2 β ,4 β ,5 α ,7 β)- (CA INDEX NAME)

Absolute stereochemistry.

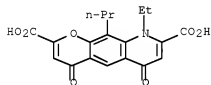
● Br⁻

10/524815

RN 34580-13-7 ZCAPLUS
 CN 10H-Benzo[4,5]cyclohepta[1,2-b]thiophen-10-one,
 4,9-dihydro-4-(1-methyl-4-piperidinylidene)- (CA INDEX NAME)



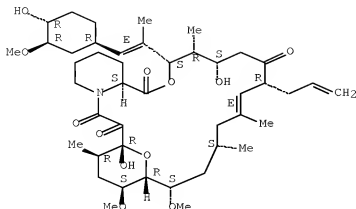
RN 69049-74-7 ZCAPLUS
 CN 4H-Pyrano[3,2-g]quinoline-2,8-dicarboxylic acid,
 9-ethyl-6,9-dihydro-4,6-dioxo-10-propyl-, sodium salt (1:2) (CA INDEX NAME)



●2 Na

RN 104987-11-3 ZCAPLUS
 CN 15,19-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclotricosine-1,7,20,21(4H,23H)-
 tetrone, 5,6,8,11,12,13,14,15,16,17,18,19,24,25,26,26a-hexadecahydro-5,19-
 dihydroxy-3-[(1E)-2-[(1R,3R,4R)-4-hydroxy-3-methoxycyclohexyl]-1-
 methylethenyl]-14,16-dimethoxy-4,10,12,18-tetramethyl-8-(2-propen-1-yl)-,
 (3S,4R,5S,8R,9E,12S,14S,15R,16S,18R,19R,26aS)- (CA INDEX NAME)

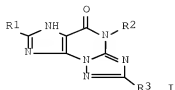
Absolute stereochemistry.
 Double bond geometry as shown.



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
(4 CITINGS)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

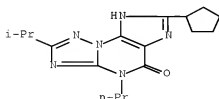
L74 ANSWER 7 OF 7 ZCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:420941 ZCAPLUS [Full-text](#)
DOCUMENT NUMBER: 133:53696
TITLE: Tricyclic nitrogen heterocycles as phosphodiesterase
IV inhibitors
INVENTOR(S): Hoffmann, Matthias; Jung, Birgit; Kuefner-Muehl,
Ulrike; Meade, Christopher John Montague
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035428	A2	20000622	WO 1999-EP9086	19991124 <--
WO 2000035428	A3	20000928		
W: CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19858331	A1	20000621	DE 1998-19858331	19981217 <--
CA 2345752	A1	20000622	CA 1999-2345752	19991124 <--
EP 1140098	A2	20011010	EP 1999-959324	19991124 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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PRIORITY APPLN. INFO.:				
			DE 1998-19858331	A 19981217 <--
			US 1999-127777P	P 19990405 <--
			WO 1999-EP9086	W 19991124 <--
OTHER SOURCE(S): MARPAT 133:53696				
GI				



- AB Tricyclic N heterocycles I [R1 = C1-5 alkyl, C5-6 cycloalkyl, Ph, PhCH2, 5- or 6-membered heterocyclic ring; R2 = C1-5 alkyl, C2-4 alkenyl; R3 = (substituted) C1-5 alkyl, (substituted) C5-6 cycloalkyl] and their salts are phosphodiesterase IV inhibitors and are potentially useful as vasodilators, inflammation inhibitors, and antiallergic agents. Thus, I (R1 = cyclopentyl, R2 = n-Pr, R3 = i-Pr) inhibited human monocyte phosphodiesterase IV with an IC50 of 0.018 μ m. A tablet formulation contained I 80, corn starch 190, lactose 55, microcryst. cellulose 35, PVP 15, Na carboxymethylstarch 23, and Mg stearate 2 mg.
- IC ICM A61K031-00
- CC 1-7 (Pharmacology)
- Section cross-reference(s): 7, 63
- IT Intestine, disease
(Crohn's; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Respiratory distress syndrome
(adult; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Eye, disease
(allergic conjunctivitis; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Bronchi
(chronic bronchitis; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Kidney, disease
(chronic glomerulonephritis; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Lung, disease
(chronic obstructive; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Granuloma
(eosinophilic; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Lung, disease
Respiratory tract
(inflammation; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Structure-activity relationship
(phosphodiesterase IV-inhibiting; of tricyclic nitrogen heterocycles)
- IT Shock (circulatory collapse)
(septic; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Allergy inhibitors

- Anti-inflammatory agents
 Anti-ischemic agents
 Antiarteriosclerotics
 Antiarthritics
 Antiasthmatics
 Antirheumatic agents
 Cystic fibrosis
 Eye, disease
 Hay fever
 Multiple sclerosis
 Psoriasis
 Urticaria
 (tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT Intestine, disease
 (ulcerative colitis; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT 9036-21-9, Phosphodiesterase IV
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT 60-92-4, CAMP
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (intracellular; tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT 252665-20-6 252665-32-0 252665-46-6 252665-52-4 259744-63-3
 259744-64-4 259744-65-5 259744-67-7 259744-68-8
 259744-69-9 259744-82-6 259744-83-7 259744-90-6 259744-91-7
 259744-95-1 259745-04-5 259745-05-6 259745-08-9 259745-18-1
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- IT 259744-67-7
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (tricyclic nitrogen heterocycles as phosphodiesterase IV inhibitors)
- RN 259744-67-7 ZCAPLUS
- CN 5H-[1,2,4]Triazolo[5,1-b]purin-5-one,
 7-cyclopentyl-4,8-dihydro-2-(1-methylethyl)-4-propyl- (CA INDEX NAME)



OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD
 (8 CITINGS)

10/524815

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his full

(FILE 'HOME' ENTERED AT 09:55:10 ON 14 OCT 2009)

FILE 'REGISTRY' ENTERED AT 09:55:15 ON 14 OCT 2009

```

L1      0 SEA SPE=ON ABB=ON PLU=ON AMITRIPTYLINE/CN
L2      1 SEA SPE=ON ABB=ON PLU=ON IMIPRAMINE/CN
        D SCA
L3      1 SEA SPE=ON ABB=ON PLU=ON AMITRIPTYLINE/CN
        D SCA
        SEL RN
        D RN L2
        D RN L3
L4      STR 50-49-7
L5      STR 50-48-6
L6      4 SEA FAM SAM L4
L7      135 SEA FAM FUL L4
L8      3 SEA FAM SAM L5
L9      83 SEA FAM FUL L5
        SAVE TEMP L7 JEA815IMIP/A
        SAVE TEMP L9 JEA815AMIT/A

```

FILE 'ZCAPLUS' ENTERED AT 10:00:52 ON 14 OCT 2009

```

L10     9293 SEA SPE=ON ABB=ON PLU=ON L7
L11     6299 SEA SPE=ON ABB=ON PLU=ON L9
        E ANTIDEPRESSANT+ALL/CT
        E E2+ALL/CT

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FILE 'REGISTRY' ENTERED AT 10:07:23 ON 14 OCT 2009

```

L12     6 SEA SPE=ON ABB=ON PLU=ON (BUTRIPTYLINE OR CLOMIPRAMINE OR
        DOSULEPIN OR DOTHIEPIN OR DOXEPIIN OR LOFEPRAMINE OR TRIMIPRAMIN
        E)/CN
        D SCA
L13     3 SEA SPE=ON ABB=ON PLU=ON (DESIPRAMINE OR NORTRIPTYLINE OR
        PROTRIPTYLINE)/CN
L14     6 SEA SPE=ON ABB=ON PLU=ON (DEMEXIPTILINE OR DIBENZEPIN OR
        DIMETACRINE OR IPRINDOLE OR MELITRACEN OR METAPRAMINE)/CN
L15     4 SEA SPE=ON ABB=ON PLU=ON (NITROXAZEPINE OR NOXIPTYLINE OR
        PROPIZEPINE OR QUINUPRAMINE)/CN
L16     6 SEA SPE=ON ABB=ON PLU=ON (AMINEPTINE OR OPIPRAMOL OR
        TIANEPTINE OR CIANOPRAMINE OR CYANODOTHIEPIN OR FLUOTRACEN)/CN
L17     25 SEA SPE=ON ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR L16)
L18     25 SEA SPE=ON ABB=ON PLU=ON L17 NOT (L7 OR L9)
        D SCA
L19     6 SEA SPE=ON ABB=ON PLU=ON (AMOXAPINE OR MAPROTIline OR
        MIANSERIN OR MIRTAZAPINE OR SETIPTILINE OR OXAPROTIline)/CN
L20     0 SEA SPE=ON ABB=ON PLU=ON L18 AND L19
        D COST

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FILE 'ZCAPLUS' ENTERED AT 10:16:36 ON 14 OCT 2009

```

        E TRICYCLIC ANTI/CT
        E E4+ALL/CT
        E E2+ALL/CT
L21     5776 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESS?/BI (L) TRICYCLIC?/BI
        E TETRACYCLIC ANTI/CT
L22     270 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESS?/BI (L) TETRACYCLIC?/BI
L23     36339 SEA SPE=ON ABB=ON PLU=ON ANTIDEPRESSANT?/BI OR ANTI

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DEPRESSANT?/BI
E CYSTIC FIBROSIS+ALL/CT
L24      15309 SEA SPE=ON ABB=ON PLU=ON ?CYSTIC FIBROS?/BI
L*** DEL 608 S FIBROCYSTIC/BI OR FIBROCYSTIC/BI
L25      609 SEA SPE=ON ABB=ON PLU=ON FIBROCYSTIC?/BI OR FIBRO CYSTIC?/BI

L26      155 SEA SPE=ON ABB=ON PLU=ON MUCOVISCIDOSIS/BI
L27      5892 SEA SPE=ON ABB=ON PLU=ON CFTR/BI
L28      15430 SEA SPE=ON ABB=ON PLU=ON FIBROSIS/BI (L) CYSTIC/BI
L29      16341 SEA SPE=ON ABB=ON PLU=ON (L24 OR L25 OR L26 OR L27 OR L28)
L30      226 SEA SPE=ON ABB=ON PLU=ON (L21 OR L22 OR L23) AND L29
L31      6 SEA SPE=ON ABB=ON PLU=ON (L21 OR L22) AND L29
L32      9 SEA SPE=ON ABB=ON PLU=ON L23 AND (TRICYCLIC?/BI OR
TETRACYCLIC?/BI) AND L29
L33      3 SEA SPE=ON ABB=ON PLU=ON L32 NOT L31
D SCA

FILE 'REGISTRY' ENTERED AT 10:28:51 ON 14 OCT 2009
L34      31 SEA SPE=ON ABB=ON PLU=ON L17 OR L19
L35      31 SEA SPE=ON ABB=ON PLU=ON L34 NOT (L7 OR L9)

FILE 'ZCAPLUS' ENTERED AT 10:29:09 ON 14 OCT 2009
L36      11 SEA SPE=ON ABB=ON PLU=ON L34 AND L29
L37      12 SEA SPE=ON ABB=ON PLU=ON (L7 OR L9) AND L29
L38      9 SEA SPE=ON ABB=ON PLU=ON L36 AND L37

FILE 'REGISTRY' ENTERED AT 10:40:10 ON 14 OCT 2009
L39      22 SEA SPE=ON ABB=ON PLU=ON L17 AND 3/NR
L40      3 SEA SPE=ON ABB=ON PLU=ON L17 NOT L39
D SCA
L41      6 SEA SPE=ON ABB=ON PLU=ON L19 AND 4/NR
D SCA

FILE 'ZCAPLUS' ENTERED AT 10:45:18 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:46:24 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 10:46:38 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:48:01 ON 14 OCT 2009
L*** DEL TRA L29 1- RN : 50127 TERMS

FILE 'REGISTRY, REGISTRY' ENTERED AT 10:48:01 ON 14 OCT 2009
L*** DEL 50126 SEA L***

FILE 'ZCAPLUS' ENTERED AT 10:50:34 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:50:56 ON 14 OCT 2009
L45      218 SEA SPE=ON ABB=ON PLU=ON L7 OR L9

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:52:26 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:52:31 ON 14 OCT 2009
SET SMARTSELECT ON
L46      SEL PLU=ON L45 1- CHEM : 409 TERMS
SET SMARTSELECT OFF

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:53:03 ON 14 OCT 2009
L47      78135 SEA SPE=ON ABB=ON PLU=ON L46
L48      96337 SEA SPE=ON ABB=ON PLU=ON L29

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10/524815

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L49      39 SEA SPE=ON  ABB=ON  PLU=ON  L47 AND L48
L50      36 DUP REM L49 (3 DUPLICATES REMOVED)
          ANSWERS '1-5' FROM FILE MEDLINE
          ANSWERS '6-34' FROM FILE EMBASE
          ANSWERS '35-36' FROM FILE BIOSIS

FILE 'EMBASE' ENTERED AT 10:55:22 ON 14 OCT 2009
L51      31 SEA SPE=ON  ABB=ON  PLU=ON  L47 AND L48
          D TRIAL 1-6

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:56:20 ON 14 OCT 2009

FILE 'REGISTRY' ENTERED AT 10:57:04 ON 14 OCT 2009
          SET SMARTSELECT ON
L52      SEL PLU=ON  L34 1- CHEM :      233 TERMS
          SET SMARTSELECT OFF

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:57:06 ON 14 OCT 2009
L53      91067 SEA SPE=ON  ABB=ON  PLU=ON  L52
L54      *** DEL 2 S L53 AND L89
L54      25 SEA SPE=ON  ABB=ON  PLU=ON  L53 AND L29
          D TRIAL 1-5
L55      54 SEA SPE=ON  ABB=ON  PLU=ON  L49 OR L54
L56      24 SEA SPE=ON  ABB=ON  PLU=ON  (TRICYCLIC OR TETRACYCLIC)/BI AND
          L29
L57      75 SEA SPE=ON  ABB=ON  PLU=ON  L49 OR L54 OR L56
          D TRIAL L56 1-5
          D TRIAL L56 6-10
L58      31 SEA SPE=ON  ABB=ON  PLU=ON  L57 AND PY<2004

FILE 'ZCAPLUS' ENTERED AT 11:05:19 ON 14 OCT 2009
L59      27 SEA SPE=ON  ABB=ON  PLU=ON  (TRICYCLIC?/BI OR TETRACYCLIC?/BI)
          AND L29
L60      7 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND PY<2004
L61      15 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND PY<2004
L62      13 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND AY<2004
L63      17 SEA SPE=ON  ABB=ON  PLU=ON  (L60 OR L61 OR L62)
          SEL RN
          DELETE SELECT
          SEL RN

FILE 'REGISTRY' ENTERED AT 11:09:34 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:09:41 ON 14 OCT 2009
L64      TRA PLU=ON  L63 1- RN :      3492 TERMS

FILE 'REGISTRY' ENTERED AT 11:09:43 ON 14 OCT 2009
L65      3492 SEA SPE=ON  ABB=ON  PLU=ON  L64
L66      1346 SEA SPE=ON  ABB=ON  PLU=ON  L65 AND NRRS>2

FILE 'ZCAPLUS' ENTERED AT 11:10:02 ON 14 OCT 2009
L67      4889 SEA SPE=ON  ABB=ON  PLU=ON  L66 AND ?DEPRESS?/BI

FILE 'REGISTRY' ENTERED AT 11:11:02 ON 14 OCT 2009
L68      1330 SEA SPE=ON  ABB=ON  PLU=ON  L66 AND NRRS<5

FILE 'ZCAPLUS' ENTERED AT 11:11:26 ON 14 OCT 2009
L69      40308 SEA SPE=ON  ABB=ON  PLU=ON  L66 (L) (THU OR DMA OR PAC OR PKT
          OR BAC)/RL
L70      788 SEA SPE=ON  ABB=ON  PLU=ON  L69 AND (?DEPRESSION? OR ?ANTIDEPRE
```

SS? OR ANTI DEPRESS?)/BI
 L71 ANALYZE PLU=ON L70 1- RN HIT : 344 TERMS
 DELETE SELECT Y
 SEL 1-344

FILE 'REGISTRY' ENTERED AT 11:15:14 ON 14 OCT 2009
 L72 344 SEA SPE=ON ABB=ON PLU=ON (50-02-2/RN OR 50-23-7/RN OR
 53-03-2/RN OR 50-24-8/RN OR 104987-11-3/RN OR 79794-75-5/RN OR
 60-87-7/RN OR 83-43-2/RN OR 51333-22-3/RN OR 378-44-9/RN OR
 76-25-5/RN OR 124-94-7/RN OR 5534-09-8/RN OR 3385-03-3/RN OR
 356-12-7/RN OR 80474-14-2/RN OR 25122-46-7/RN OR 50-03-3/RN OR
 67-73-2/RN OR 382-67-2/RN OR 1247-42-3/RN OR 3093-35-4/RN OR
 426-13-1/RN OR 638-94-8/RN OR 2152-44-5/RN OR 1524-88-5/RN OR
 34580-13-7/RN OR 33564-31-7/RN OR 52-39-1/RN OR 67-78-7/RN OR
 50-04-4/RN OR 51022-69-6/RN OR 2668-66-8/RN OR 49697-38-3/RN
 OR 66575-29-9/RN OR 83919-23-7/RN OR 969-33-5/RN OR 13609-67-1/
 RN OR 152-97-6/RN OR 2135-17-3/RN OR 53-34-9/RN OR 53-36-1/RN
 OR 23674-86-4/RN OR 5593-20-4/RN OR 57524-89-7/RN OR 125-02-0/R
 N OR 2002-29-1/RN OR 2375-03-3/RN OR 3693-39-8/RN OR 66734-13-2
 /RN OR 41767-29-7/RN OR 508-99-6/RN OR 52-21-1/RN OR 125-04-2/R
 N OR 14484-47-0/RN OR 56-47-3/RN OR 59198-70-8/RN OR 73771-04-7
 /RN OR 987-24-6/RN OR 25122-57-0/RN OR 30286-75-0/RN OR
 312-93-6/RN OR 3801-06-7/RN OR 1110-40-3/RN OR 1255-35-2/RN OR
 1597-82-6/RN OR 22298-29-9/RN OR 2825-60-7/RN OR 514-36-3/RN
 OR 5611-51-8/RN OR 599-33-7/RN OR 66852-54-8/RN OR 69049-74-7/R
 N OR 82-88-2/RN OR 1177-87-3/RN OR 19888-56-3/RN OR 34097-16-0/
 RN OR 50629-82-8/RN OR 5251-34-3/RN OR 4330-99-8/RN OR
 151-73-5/RN OR 2392-39-4/RN OR 55560-96-8/RN OR 7681-14-3/RN
 OR 86-74-8/RN OR 1229-35-2/RN OR 2920-86-7/RN OR 35100-44-8/RN
 OR 58497-00-0/RN OR 58524-83-7/RN OR 6000-74-4/RN OR 1107-99-9/
 RN OR 125-03-1/RN OR 125-10-0/RN OR 132-65-0/RN OR 1715-33-9/RN
 OR 20423-99-8/RN OR 2265-64-7/RN OR 29205-06-9/RN OR 2921-57-5
 /RN OR 303-40-2/RN OR 5060-55-9/RN OR 630-67-1/RN OR 778576-34-
 4/RN OR 778576-35-5/RN OR 778576-36-6/RN OR 778576-37-7/RN OR
 778576-38-8/RN OR 778576-39-9/RN OR 778576-40-2/RN OR 778576-41
 -3/RN OR 778576-42-4/RN O

FILE 'ZCAPLUS' ENTERED AT 11:15:54 ON 14 OCT 2009
 L73 8 SEA SPE=ON ABB=ON PLU=ON L72 AND L63
 D OCC 1-
 L74 7 SEA SPE=ON ABB=ON PLU=ON (L72 (L) (THU OR DMA OR BAC OR PKT
 OR PAC)/RL) AND L63
 D OCC 1-
 D SCA
 L75 227 SEA SPE=ON ABB=ON PLU=ON GULBINS E7/AU, AUTH
 L76 6 SEA SPE=ON ABB=ON PLU=ON L75 AND (L7 OR L9 OR L17 OR L19)
 L77 18 SEA SPE=ON ABB=ON PLU=ON L75 AND L29

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:20:43 ON 14 OCT 2009
 L78 24 SEA SPE=ON ABB=ON PLU=ON L75 AND (L47 OR L53)
 L79 48 SEA SPE=ON ABB=ON PLU=ON L75 AND L29
 L80 64 SEA SPE=ON ABB=ON PLU=ON L78 OR L79
 L81 32 DUP REM L80 (32 DUPLICATES REMOVED)
 ANSWERS '1-21' FROM FILE MEDLINE
 ANSWERS '22-24' FROM FILE EMBASE
 ANSWERS '25-32' FROM FILE BIOSIS

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:22:08 ON 14 OCT 2009
 L82 8 SEA SPE=ON ABB=ON PLU=ON L57 AND L75


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FILE 'ZCAPLUS' ENTERED AT 11:22:35 ON 14 OCT 2009
L83      14 SEA SPE=ON  ABB=ON  PLU=ON  L75 AND L32 OR L36 OR L37
L84      2 SEA SPE=ON  ABB=ON  PLU=ON  L75 AND (L32 OR L36 OR L37)
L85      0 SEA SPE=ON  ABB=ON  PLU=ON  L75 AND L74
L86      0 SEA SPE=ON  ABB=ON  PLU=ON  L59 AND L75

FILE 'REGISTRY' ENTERED AT 11:24:11 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:24:13 ON 14 OCT 2009
      D STAT QUE L76
      D STAT QUE L77
      D STAT QUE L84
L87      22 SEA SPE=ON  ABB=ON  PLU=ON  L76 OR L77 OR L84

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:24:54 ON 14 OCT 2009
      D STAT QUE L78
      D STAT QUE L79
      D STAT QUE L82
L88      64 SEA SPE=ON  ABB=ON  PLU=ON  L78 OR L79 OR L82

FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:25:25 ON 14 OCT 2009
L89      37 DUP REM L87 L88 (49 DUPLICATES REMOVED)
          ANSWERS '1-22' FROM FILE ZCAPLUS
          ANSWERS '23-29' FROM FILE MEDLINE
          ANSWERS '30-32' FROM FILE EMBASE
          ANSWERS '33-37' FROM FILE BIOSIS
      D IBIB ABS HITIND HITSTR L89 1-22
      D IALL L89 23-37

FILE 'REGISTRY' ENTERED AT 11:26:43 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:26:46 ON 14 OCT 2009
      D STAT QUE L32
      D STAT QUE L36
      D STAT QUE L37
L90      22 SEA SPE=ON  ABB=ON  PLU=ON  L32 OR L36 OR L37

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:27:21 ON 14 OCT 2009
      D STAT QUE L58

FILE 'ZCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:27:33 ON 14 OCT 2009
L91      49 DUP REM L90 L58 (4 DUPLICATES REMOVED)
          ANSWERS '1-22' FROM FILE ZCAPLUS
          ANSWERS '23-27' FROM FILE MEDLINE
          ANSWERS '28-48' FROM FILE EMBASE
          ANSWER '49' FROM FILE BIOSIS
      D IBIB ABS HITIND HITSTR L91 1-22
      D IALL L91 23-49

FILE 'REGISTRY' ENTERED AT 11:28:47 ON 14 OCT 2009

FILE 'ZCAPLUS' ENTERED AT 11:28:55 ON 14 OCT 2009
      D STAT QUE L74
      D IBIB ABS HITIND HITSTR L74 1-7

FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file

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provided by InfoChem.

STRUCTURE FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6
DICTIONARY FILE UPDATES: 12 OCT 2009 HIGHEST RN 1187916-70-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdnoc/properties.html>

FILE ZCAPLUS

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FILE COVERS 1907 - 14 Oct 2009 VOL 151 ISS 16
FILE LAST UPDATED: 13 Oct 2009 (20091013/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

ZCaplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE MEDLINE

FILE LAST UPDATED: 13 Oct 2009 (20091013/UP). FILE COVERS 1949 TO DATE.

MEDLINE and LMedLINE have been updated with the 2009 Medical Subject
Headings (MeSH) vocabulary and tree numbers from the U.S. National Library
of Medicine (NLM). Additional information is available at

http://www.nlm.nih.gov/pubs/techbull/nd08/nd08_medline_data_changes_2009.

On February 21, 2009, MEDLINE was reloaded. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

See HELP RANGE before carrying out any RANGE search.

FILE EMBASE

FILE COVERS 1974 TO 14 Oct 2009 (20091014/ED)

EMBASE was reloaded on March 30, 2008.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 7 October 2009 (20091007/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

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